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To My Wife

JUNE-80

Preface

The revisions to the First Edition consist of (1) an integration of aliphatic nd aromatic chemistry, (2) the incorporation of physical with chemical methods of structure determination, (3) the inclusion of more reaction mechanisms, (4) answers to the Test Questions, (5) the strengthening of certain topics such as alicyclic chemistry, and (6) where appropriate, a general up-dating of material.

As in the first edition, the objective of this book is to serve as a textbook for elementary organic chemistry. Consequently, only fundamental treatments are given to such specialized topics as synthetic dyes, steroids, alkaoids, terpenes, carbohydrates, and proteins, because a full examination of such topics would require expanded applications of the basic principles of organic chemistry and would be more than the student could learn in one year. Most of the contents of this book can be covered in the conventional one-year course. Advanced students wishing to review their elementary organic chemistry will find the study guides appearing throughout the book of considerable help.

Structural theory was employed during the early stages of organic chemstry to interpret and explain organic reactions. This theory was based on he functional groups present in a molecule. In the past quarter-century, ncreasing attention has been given to reaction mechanisms and charge-ensity patterns of molecules. This has facilitated an understanding and redictability of the properties of organic molecules. Although certain heoretical approaches have been fairly successful in characterizing some molecules, most chemists have had to rely upon the old structural theory, with a judicious incorporation of the concepts of molecular orbitals, hybridiation, resonance, induction, hydrogen bonding, and steric requirements. This multi-effect approach, referred to as the "modern structural thoery,"[1] is also pplied in this book. These auxiliary concepts are woven into a uniform eatment and explained when first encountered, so that the student recognizes their usefulness for interpreting the behavior of organic compounds.

There have been two major approaches used in the study of organic hemistry. One is to classify organic compounds on the basis of functional groups. With this knowledge one could predict the properties of a compound if its structure is known or, conversely, deduce its structure on a basis of its properties. The second approach is to teach certain mechanistic ways in which organic moelcules tend to react. An understanding of these reaction types would enable the student to predict the behavior of any organic compound under given conditions. In both approaches there can be considerable memory work for the student unless a rational basis is used for correlating the material. This book takes a position between these two extreme approaches. The author believes that a knowledge of the common chemical and physical properties of functional groups enables the student to retain a vast amount of information. At the same time, his understanding of the mechanisms of certain pervalent reactions extends his grasp of organic chemistry to include complex substances in which functional group properties are somewhat altered.

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[1] L. N. Ferguson, *Modern Structural Theory of Organic Chemistry*, Prentice-Hall, Inc., nglewood Cliffs, N.J., 1963.

A student must understand the basic concepts and principles taken up here in order to become familiar with the nature of organic substances and to appreciate their potential. By going through the mental exercises called for, the student understands the scientific approach, and develops his capacity for reasoning and solving problems encountered later in chemistry as well as in specialized fields such as medicine, agriculture, and engineering.

Throughout the book there are question sets of two types. One, the Study Exercises, consists essentially of drill questions aimed at improving the student's proficiency in performing some of the operations discussed in the chapter. These questions help familiarize him with the subject matter and impress it firmly in his memory. The Test Questions, for which answers are supplied at the back of the book, are designed to challenge the student's integrated impressions from the entire course up to that point, with emphasis on the part most recently discussed. This gives an evaluation of what he has learned. These questions require much more than looking up the answers in the text; they call for logical reasoning or analytical thinking and tend to coordinate the subject matter. Another feature of this book are frequent comments on historical or cultural items of interest. These are set off in smaller type.

In the Appendix there is a section devoted to the solution of mathematical problems encountered in organic chemistry for the benefit of those students who need a brush-up of this type.

I am indebted to many persons for various suggestions that have been incorporated into this revision, and to Richard W. Dempsey for the full-page drawings on pages 74 and 626. Also, I thank the College of Liberal Arts of Howard University for providing clerical assistance in typing the final manuscript. I want to express my deep appreciation to my wife for her forbearance during the preparation of this revision.

LLOYD N. FERGUSON

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A Word to the Student

The phenomenal success of science is due largely to its hierarchical nature. It has a simple foundation of a relatively few abstract concepts and principles, and upon these primordial elements is constructed a vast, complex superstructure of facts and applications. The myriad of facts in any discipline of this edifice of science would overwhelm the human mind were it not for the logical, sequential thread of continuity joining the network of details.

In the same sense, organic chemistry would be a hopeless maze if it could not be presented within an orderly, rational framework. More than a million organic compounds have been prepared, and it would take a lifetime to become familiar with all of them. What should be sought in this study of organic chemistry, then, is the attainment of a knowledge of the general nature of organic substances without an intimate acquaintance with each of them.

The task of the teacher is to help the student achieve this objective. He does this by discussing, among other aspects of organic chemistry, some of the basic properties of organic substances. The aim is to develop in the student a sense for the behavior of an organic compound when affected by physical forces such as light, heat, electric or magnetic fields, and other chemicals. Under given conditions, will a specific compound be inert or reactive, and if reactive, how will it react? Such knowledge will lead to one of the objectives of most chemists: to be able to predict the chemical and physical properties of any compound if its molecular structure is known, and, conversely, to be able to design the structure of a substance that would have a specifically desired property. We would then know, for example, what substance to use in making the parts for space vehicles that must withstand extreme heat, or what drug to use for a specific disease.

A common method of teaching organic chemistry is to present it as it is used by an organic chemist. With this method the nomenclature, synthesis, isolation, properties, methods of structure determination, and uses of organic compounds are taken up. This approach gives the student an appreciation for the way that advances are made in organic chemistry and reduces rote memory work. Memorization is sometimes considered to be the principle difficulty in organic chemistry. It is true that in order to plan a multistep synthesis with dispatch, or to distinguish several compounds on the basis of differences in their chemical properties, one must know a basic group of organic reactions. It is this "working pool" of reactions that the student must somehow commit to memory. But rote memorization is reduced by associating the reactions with various operations and end uses such as resolution of mixtures, formation of derivatives, qualitative identification, and structure determination. Without special efforts to memorize the reactions or their mechanisms, the student learns them as a result of associating them with specific uses.

All this material is interrelated by the fiber of theory and by the basic principles of organic chemistry. Some theory must be learned, of course, in order to provide a structural framework for organic chemistry. Actually it is not expected that the student will remember long after the course all the many reactions taken up, their mechanisms, and other details presented. The objective of the course will be achieved if he learns the hierarchical structure of organic chemistry, understands the relations between the basic theory and factual detail, and experiences some of the mental processes used by organic chemists. Organic substances play such a large role in our daily lives that all of us should know something about organic chemistry in order to understand some of the ways in which it affects us and to appreciate its potentials and limitations.

All temperatures in this book are given in degrees centigrade (°C) unless otherwise noted.

1

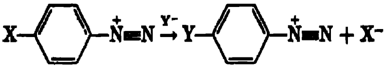
The Structures of Organic Molecules

1.1 CHEMICAL BONDS

a. Atomic orbitals. For many years chemists have sought relationships between the chemical constitution of matter and its physical, chemical, and biochemical properties, in order to be able to predict the properties of a compound when its chemical structure is known, and conversely, in order to be able to plan the structure of a compound which would have any desired properties. The most powerful correlation that has been found is the periodic table of the elements, which is based on the magnitude of the nuclear charge and the arrangements of the orbital electrons revolving around the nuclei. In order to account for observed properties, such as ionization potentials, magnetic susceptibilities, valences, and periodicity of chemical properties, it is believed that electrons move around atomic nuclei in discrete, successive, concentric volumes called *shells*. Each shell will accommodate a definite number of electrons, and the electrons are most likely to be found in definite regions, called *orbitals*, within each shell. These orbitals are of four types, distinguishable by their geometric shapes and the angular momentum an electron will exhibit when located in a given type of orbital. The orbital types are referred to as *s*, *p*, *d*, and *f* orbitals.

Based on experimental data, mostly spectroscopic and magnetic, and from theoretical considerations, electron distributions have been assigned to all elements in accordance with the following five principles:

1. Each shell will hold up to $2n^2$ electrons, where n is the shell number or principal quantum number. There may be one *s*, three *p*, five *d*, and seven *f* orbitals in each shell, depending on how many are needed to accommodate $2n^2$ electrons.
2. The electrons will enter the available orbital of lowest energy.
3. At any one energy level, the electrons will tend to occupy separate orbitals.
4. Only two electrons can be in the same orbital, provided their spins are antiparallel.



TEST QUESTIONS, Set 16

1. What is the pH of a 0.1 N aqueous solution of diethylamine? $K_b = 1.26 \times 10^{-3}$.

2. Indicate the sequence of reactions one could use in the laboratory to convert propyl iodide into propylamine, and what weight of propylamine could be produced from 17 g of propyl iodide if each step takes place in a 90% yield?

3. Work problem 2 for the conversion of propyl iodide into n-butylamine.

4. What volume of nitrogen gas, measured at 745 mm and 25°, will be collected if 0.15 g of butylamine is treated with nitrous acid, and the nitrogen is collected with 98% efficiency?

5. What is the molecular weight of a monoamine if a 0.22-g sample produces 59.9 ml of N_2, measured at 25° and 738 mm, assuming the per cent efficiency of collection of nitrogen is 95%?

6. A 10-g sample of urine was treated with nitrous acid and the N_2 collected over concentrated KOH. When the volume of the gas was corrected to standard conditions, it was found to occupy a volume of 89.6 ml. What was the percentage of urea, $(H_2N)_2CO$, in the sample?

7. What is the concentration of hydroxide ion in 200 ml of an aqueous solution containing 5 g of isoamylamine? $K_b = 5 \times 10^{-4}$.

8. How could one separate and isolate the components in a mixture of octanoic acid, n-octylamine, and 2-octanol without resorting to fractional distillation other than the separation from ether or chloroform?

9. What series of laboratory reactions could be used to convert methyl n-propyl ketone to n-propylamine?

10. What are two different qualitative test-tube experiments which could be used to distinguish pure samples of the isomeric amines, n-pentylamine and ethyl-n-propylamine?

11. Indicate the series of reactions one could use in the laboratory to prepare each of the following, starting with benzene in each case: (a) m-chloroaniline; (b) m-fluorobenzoic acid; (c) 3,4′-dimethylbiphenyl; (d) 3-iodo-4′-methylazobenzene; (e) 4-chloro-4′-bromoazobenzene; (f) m-bromobiphenyl; (g) 2,6-dinitrophenol; (h) 3,3′-diiodoazobenzene; (i) o-dinitrobenzene; (j) 1,3,5-tribromobenzene.

12. How could one separate and isolate the components in the following mixtures without using fractional distillation other than the separation from ether: (a) salicylaldehyde, p-hydroxybenzaldehyde, N-methylaniline, benzaldehyde, and toluene; (b) p-chlorophenol, p-chloroaniline, p-chloro-N-methylaniline, and p-chloronitrobenzene?

13. How can the following be distinguished by qualitative test-tube experiments: (a) $C_6H_5NH_3Cl$ from $Cl—C_6H_4—NH_2$, (b) $CH_3—C_6H_4—NH_2$ from $C_6H_5NHCH_3$?

14. Starting with a substituted nitrobenzene, how could 3,3′-diethylbiphenyl be prepared in the laboratory?

15. If a water solution of benzenediazonium chloride shows the presence of chloride ion and is neutral, what is known regarding the strength of the base benzenediazonium hydroxide, $\phi N_2^+OH^-$?

16. What weight of iron is necessary to reduce 100 g of nitrotoluene to toluidine in acid solution?

17. What is the relative order of basicity of aniline, p-nitroaniline, N-methylaniline, and cyclohexylamine?

18. Offer an explanation for the observation that benzenediazonium chloride does

spite of the larger nuclear charges, the electrons are more easily removed from the 2*s* orbitals than the 1*s* orbitals of hydrogen and helium. The ionization potential of the next element, boron, is a little less than that of beryllium, owing to the greater distance of the 2*p* orbital from the nucleus. The potentials of carbon and nitrogen increase over that of boron because of the greater nuclear charges. However, the 2*p* orbitals of nitrogen are half filled, whereas they are more than half filled for oxygen. In spite of the greater nuclear charge of oxygen, it is easier to remove an electron from oxygen than from nitrogen. This fact supports principle 5 above. In similar fashion, the five principles above are found to account for the ionization potentials of all the elements.

b. Shapes of atomic orbitals. The atomic *s* orbitals are spherically symmetrical about the nucleus as shown in Figure 1.1.

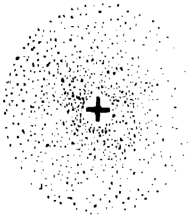


Fig. 1.1. Representation of an atomic *s* orbital. The nucleus is designated by +.

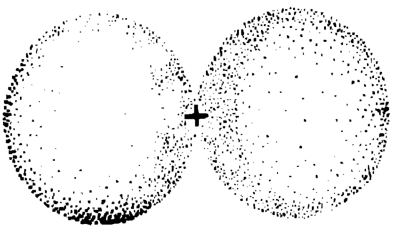


Fig. 1.2. Shape of an atomic *p* orbital. The position of the nucleus is designated by +.

It must be kept in mind that an orbital is a particularly shaped *region in space* within which electrons are likely to be found. All *s* orbitals are spherical, being concentric about the nucleus. Thus, the 2*s* orbital surrounds the 1*s* orbital.

A *p* orbital has the shape shown in Figure 1.2. Each *p* orbital has two spheres just tangent at the nucleus. The three *p* orbitals in any given shell are mutually perpendicular as the cartesian coordinates, and are referred to as p_x, p_y, and p_z orbitals. See Figure 1.3. The *d* and *f* orbitals are more varied and complex in shape.

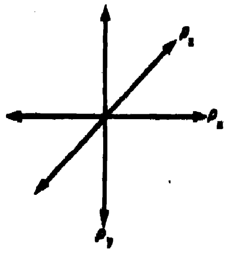


Fig. 1.3.

c. Bond formation. To explain the valences of many of the elements, it was proposed independently by the German chemist W. Kossel and by the American chemist G. N. Lewis in 1916 that the elements strive to acquire the electron distributions of the nearest inert elements. This idea is easy to accept because the inert elements resist entering into chemical combination. There must be something about their electronic structures that gives them optimum stability, and the feature they have in common is eight electrons in their outermost orbits (except helium, which has only two altogether). Sodium is eager to lose its outer electron to acquire the closed-shell distribution or octet of outer electrons, like that of neon, resulting in an ion with a unit positive charge. Sodium, therefore, is said to have an electrovalence of +1. By the same reasoning, the most common electrovalence of chlorine is −1, because it seeks one electron to acquire the octet of outer electrons like that of argon.

Now, if these two elements, sodium and chlorine, were allowed to react in some way, they would vigorously accommodate each other, sodium releasing its electron to chlorine, resulting in the two ions, Na^+ and Cl^-. These ions would attract each other by *coulombic attraction* (the name of the force by which oppositely charged particles attract each other and like-charged particles repel each other) to form the stable salt, NaCl. In the same fashion, two chlorine atoms could each acquire an electron from magnesium, which is anxious to give up two electrons, to form the Mg^{++} and two Cl^- ions. These, of course, would be attracted by coulombic forces to form the salt $Cl^-Mg^{++}Cl^-$, or $MgCl_2$. These ionic charges, resulting from the complete loss or gain of electrons, are referred to as *electrovalences*.

The novel idea of Lewis in 1916 was that atoms may also acquire electrons on a part-time basis by sharing them with other atoms. For example, each hydrogen atom seeks another electron to have two like the inert element helium. When two hydrogen atoms bond to form the hydrogen molecule, their atomic *s* orbitals overlap, and the two electrons pair up to move about in a new orbital called a *molecular orbital*. Within this new orbital each electron is electrostatically attracted to two nuclei instead of one, and as a result, the hydrogen molecule is more stable than two isolated hydrogen atoms by 103 kcal/mole. This explains the energy of such a bond, called a *covalent bond*. It can be seen that the bonding energy is really due to electrostatic forces.

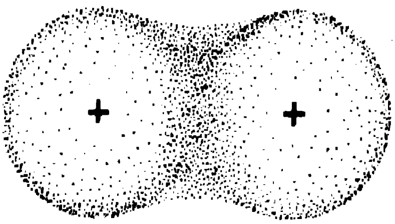


Fig. 1.4. Cross-sectional view through the nuclei of the *s-s* molecular orbital of the hydrogen molecule.

Like atomic orbitals, molecular orbitals can accommodate only two electrons, and then only if the electron spins are antiparallel. The more the atomic orbitals of two nuclei can overlap, the stronger is the covalent bond.

In the same fashion as hydrogen, other elements try to acquire electron distributions of inert elements by sharing electron pairs. Since the covalent bonds arise by each atom donating one electron to form a shared pair, the number of orbitals about an atom containing an unpaired electron will determine the covalence of the element. For illustration, the covalences of 3, 2, 2, and 1 for nitrogen, oxygen, sulfur, and fluorine, respectively, are predictable from their electron distributions shown in Table 1.1.

d. Covalent bond angles. Since an *s* orbital is spherical, it can overlap another orbital equally in all directions and the tendency to bond is equal in all directions. The *p* orbitals are mutually perpendicular to each other, and therefore their overlap with other orbitals is greatest in directions normal to each other. Consequently, elements using *p* orbitals, such as nitrogen, oxygen, and sulfur tend to form bonds making angles of 90° with each other, as illustrated in Figure 1.5. By actual measurement (cf. Section 6.1), the H—S—H bond angle of H_2S is 92° 20′.

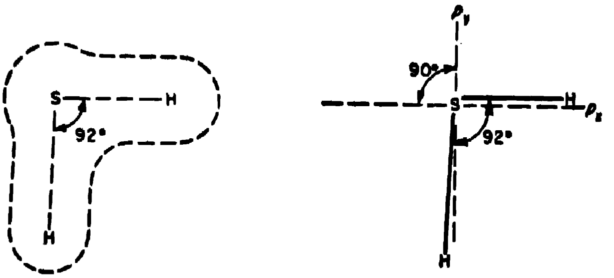


Fig. 1.5. Representation of the molecular orbitals in the H_2S molecule.

Oxygen, too, should form bonds making an angle of 90° with each other, but the angle is found to be 100° in F_2O and 105° in H_2O. This discrepancy is due to the repulsion between the atoms attached to oxygen, which spreads the bond angles. When attached to the larger sulfur atom in H_2S, the two hydrogen atoms are farther apart, so that there is less repulsion between them and they distort the normal bond angle less.

In the electron configurations of phosphorus and nitrogen, each element has 3 unpaired *p* electrons. Hence, these two elements should be tricovalent with interbond angles of 90°. In PH_3, the H—P—H bond angles are 93°, whereas in NH_3, the H—N—H bond angles are 106°. Here again, spatial requirements about the smaller nitrogen atom cause larger bond angles about nitrogen than are found about phosphorus.

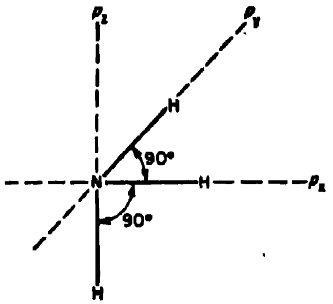


Fig. 1.6. Theoretical bond angles about nitrogen in NH_3.

e. Hybridization of bond orbitals. According to the electron distribution of carbon, $1s^22s^22p^2$, carbon should be *dicovalent*. However, in all stable compounds of carbon it is found to have a covalence of 4. To account for this fact, Linus Pauling proposed that atomic orbitals about an atom may merge or *hybridize* to form composite or hybrid orbitals. Thus, if carbon promotes one of its 2*s* electrons to a 2*p* orbital, the 2*s* and three 2*p* orbitals may merge to form four sp^3 hybrid orbitals, each containing 1 electron. This process enables carbon to form four equivalent covalent bonds instead of only two, thereby leading to more stable compounds. The energy necessary to promote the 2*s* electron to a 2*p* orbital is offset by the greater stability of sp^3-type bonds over *p*-type bonds and the larger number of bonds which can be formed. It can be deduced that carbon does not promote the 2*s* electron to the 2*p* orbital and then form one *s* and three *p* covalent bonds, because then one bond would be different from the other three. To the contrary, it is well established that the four carbon bonds in a simple molecule like CH_4 or CCl_4 are identical.

Furthermore, it is found that four sp^3 hybrid bonds form angles of 109.5° with each other (in the absence of interatomic repulsive forces, which may distort these angles as they do in H_2O). See Figure 1.7.

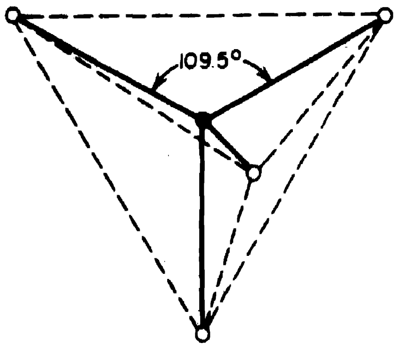


Fig. 1.7a. Four sp^3 hybrid bonds point to the apices of a tetrahedron.

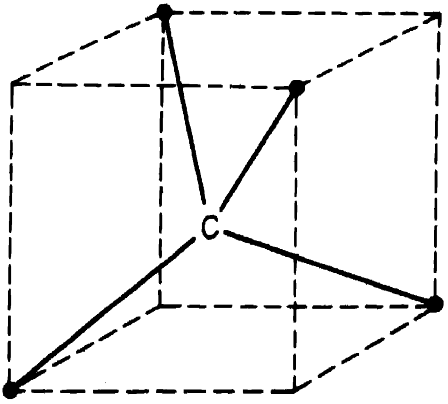


Fig. 1.7b. A tetrahedron fits into a cube with apices at opposite corners of a cube.

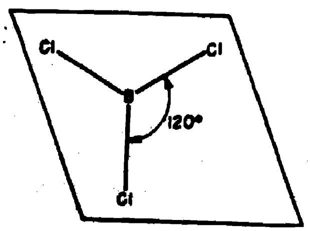
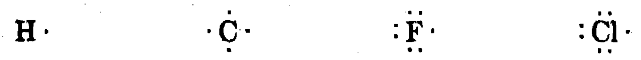


Fig. 1.8. Bond angles in BCl_3

In a similar way, boron may promote one of its 2*s* electrons to a 2*p* orbital, and then the 2*s* and two 2*p* orbitals can merge to form three sp^2 hybrid orbitals. This accounts for the fact that boron is tricovalent rather than unicovalent. For instance, BCl_3 is a gas at room temperature, having a melting point of −107° and a boiling point of 13°. Hybrid sp^2 orbitals form coplanar bond angles of 120°. See Figure 1.8.

In order to depict molecules in which the atoms are joined by covalent bonds, structural formulas are drawn. It is conventional to let the symbol for an element represent its kernel, that is, an atom of the element less its valence electrons (the outermost electrons, which are involved in chemical reactions). Hence, atoms of some of the first few elements are drawn as follows:

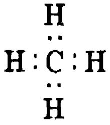


$$\mathrm{H}\cdot \qquad \cdot\underset{\cdot}{\dot{\mathrm{C}}}\cdot \qquad :\underset{..}{\ddot{\mathrm{F}}}\cdot \qquad :\underset{..}{\ddot{\mathrm{Cl}}}\cdot$$

Hydrogen Carbon Fluorine Chlorine

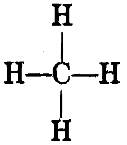
The dots indicate valence electrons. Molecular chlorine is drawn as $:\underset{..}{\ddot{\mathrm{Cl}}}:\underset{..}{\ddot{\mathrm{Cl}}}:$.

The covalent bond is conventionally designated by a dash; hence, Cl_2 is drawn as $:\underset{..}{\ddot{\mathrm{Cl}}}{-}\underset{..}{\ddot{\mathrm{Cl}}}:$, or more commonly as Cl—Cl. Similarly, CH_4 is drawn as



$$\begin{array}{c}\mathrm{H}\\ \cdot\cdot\\ \mathrm{H:C:H}\\ \cdot\cdot\\ \mathrm{H}\end{array}$$

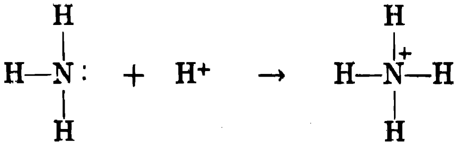
or simply as



$$\begin{array}{c}\mathrm{H}\\ |\\ \mathrm{H{-}C{-}H}\\ |\\ \mathrm{H}\end{array}$$

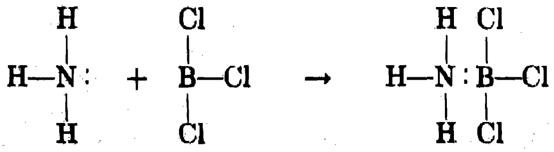
In such a compound, called *methane*, the carbon has formed four covalent bonds, giving it a covalence of 4; each hydrogen atom has a covalence of 1. Notice that there is no charge associated with covalence, just a number. Accordingly, the covalences of nitrogen, oxygen, and fluorine are 3, 2, and 1, respectively. More will be said about covalent bonds and the covalences of the first few elements in Section 1.4.

It is noteworthy that some atoms readily share their electron pairs with other atoms to help the latter acquire rare-gas electron distributions. For example, nitrogen in ammonia has an unshared pair of electrons (in its 2*s* orbital) that it shares with a proton to form the ammonium ion.



$$\begin{array}{c}\mathrm{H}\\ |\\ \mathrm{H{-}N{:}}\\ |\\ \mathrm{H}\end{array} + \mathrm{H}^+ \rightarrow \begin{array}{c}\mathrm{H}\\ |^{+}\\ \mathrm{H{-}N{-}H}\\ |\\ \mathrm{H}\end{array}$$

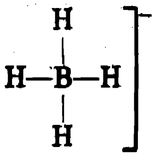
Now, the proton has two electrons at least part of the time and the nitrogen still has eight part of the time. The combined stability of the ammonium ion is greater than that of the separate ammonia molecule and proton. In the same way, the nitrogen atom of ammonia readily shares its lone-pair electrons with the boron atom of BCl_3, in order that the boron atom may have an outer octet at least part of the time (it has a vacant 2*p* orbital, and therefore it can accommodate an additional electron pair).



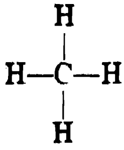
$$\begin{array}{c}\mathrm{H}\\ |\\ \mathrm{H{-}N{:}}\\ |\\ \mathrm{H}\end{array} + \begin{array}{l}\mathrm{Cl}\\ |\\ \mathrm{B{-}Cl}\\ |\\ \mathrm{Cl}\end{array} \rightarrow \begin{array}{cl}\mathrm{H} & \mathrm{Cl}\\ | & |\\ \mathrm{H{-}N{:}} & \mathrm{B{-}Cl}\\ | & |\\ \mathrm{H} & \mathrm{Cl}\end{array}$$

The bond between nitrogen and boron is essentially covalent, and is called a *coordinate covalent bond*. This term denotes that 1 atom donated both electrons of the shared electron pair, whereas a *covalent* bond is one formed between two atoms to which each atom contributed equally.

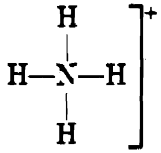
Simple boron compounds are planar, and ammonia is pyramidal, but when boron and nitrogen form four covalent bonds, they assume tetrahedral configurations like carbon.



$$\left[\begin{array}{ccc} & H & \\ & | & \\ H- & B & -H \\ & | & \\ & H & \end{array}\right]^-$$



$$\begin{array}{ccc} & H & \\ & | & \\ H- & C & -H \\ & | & \\ & H & \end{array}$$

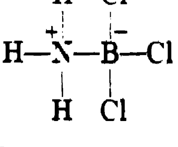


$$\left[\begin{array}{ccc} & H & \\ & | & \\ H- & N & -H \\ & | & \\ & H & \end{array}\right]^+$$

Boron changes from sp^2 to sp^3 bonding, and nitrogen changes from p to sp^3 bonding. It is evident that hybridization has occurred in the ammonium ion, for if it had not, three of nitrogen's bonds would be using p orbitals and one would be using an s orbital. One hydrogen atom would then have different properties from the other three, but this is not observed.

Lewis recognized the tendency of certain substances to share their electron pairs readily and the tendency of other atoms to accept and share an electron pair readily. He called the electron donors *bases*, and the electron-pair acceptors *acids*. This concept provides the most widely applicable theory of acids and bases and is referred to as the *Lewis theory* or *electronic theory* of acids and bases.

Often when a coordinate covalent bond is formed, charges arise on the two atoms involved. For instance, in the ammonia-boron trichloride salt above, when the nitrogen atom of ammonia shares its electron pair with the boron atom, the nitrogen loses a portion of the negative charge normally found near its nucleus. At the same time there is an increase in negative charge about the boron nucleus. This creates a fraction of a unit positive charge on the nitrogen and a fractional negative charge on the boron, which charges are referred to as *formal charges*. Hence, the structure of the salt is more correctly written



$$\begin{array}{cccc} & H & Cl & \\ & | & | & \\ H- & \overset{+}{N} & -\overset{-}{B} & -Cl \\ & | & | & \\ & H & Cl & \end{array}$$

Another way of understanding how these formal charges arise is as follows: The nitrogen atom is regarded as having all 8 electrons revolving around it part of the time and the rest of the time these same shared pairs of electrons are revolving around the other 4 atoms, leaving none for nitrogen. The time-average number of electrons about nitrogen, then, is 4. Nitrogen wants 5 in its valence shell for electrical neutrality (charge of +7 on nucleus, −2 in first orbit, hence, −5 in outer orbit), and therefore the time-average number of 4 gives it a residual unit positive charge. The boron too will have a time-average number of 4 electrons about it, but it wants only 3 for neutrality (+5 on nucleus, −2 in first orbit, hence, −3 in outer orbit). Therefore, the time-average number of 4 electrons about boron gives it a residual unit negative charge.

In general, one-half of the electrons of a covalent bond may be considered as belonging to each atom forming the bond. A *formal charge*, then, is the resultant of the kernel charge and the charge of the surrounding electrons after equal distribution of shared electrons. The charge on the kernel is always positive and equal to the number of valence electrons. This usually turns out to be equal to the number of the group to which the atom belongs in the periodic table. Thus, for hydrogen, carbon, nitrogen, oxygen, and the halogens, the kernel charges are +1, +4, +5, +6, and +7, respectively.

1.2 IONIC AND COVALENT COMPOUNDS

In the previous section, it was found that the atoms in some substances are held together by coulombic attraction between oppositely charged ions, and that such binding forces are called *electrovalent* or *ionic bonds*. On the other hand, in some compounds the atoms are joined through shared electron pairs, and such bonds are called *covalent bonds*. These are the two principal types of chemical bonds, and it will be helpful to compare the general properties of ionic substances with those of covalent compounds. The broad comparisons are made in Table 1.2 and each comparison i~ discussed below.

TABLE 1.2. COMPARISON OF IONIC WITH COVALENT SUBSTANCES

	Ionic	*Covalent*
1.	Usually inorganic	Commonly organic
2.	High melting and boiling points	Low melting and boiling points
3.	Sol. H_2O; insol. organic liquids	Sol. organic liquids; insol. H_2O
4.	Conduct electric current in molten state and in solution	Solutions and melts nonconducting
5.	Hard to burn	Burn readily
6.	Reactions ionic, rapid, and simple	Reactions molecular, slow, and complex
7.	From any of 103 elements, numbering about 100,000	Mostly from 10 elements, numbering about 1,000,000
8.	Bonds between like elements rare and isomerism unusual	Bonds between carbon atoms typical and isomerism common

Comparison No. 1: Earlier it was stated that organic substances are those containing carbon, and that inorganic substances are those which do not contain carbon. Naturally, there are exceptions and borderline cases for all the comparisons made in Table 1.2. Right here, for instance, the student may think of carbon-containing sodium carbonate and potassium cyanide among the inorganic substances he studied in general chemistry. Such substances, however, can be obtained from mineral deposits, and their properties are so related to those of inorganic chemicals that it is advantageous to group them with the inorganic substances. Then too, quite a number of covalent compounds do not contain carbon, such as the MX_4 and MH_4 compounds of group IV in the periodic table, where M is Si, Sn, Ge, or Pb, and X is a halogen. Nevertheless, the covalent compounds which do contain carbon outnumber the other covalent compounds by manyfold and are of such greater importance that the comparisons made in Table 1.2 are useful. The distinction between organic and inorganic substances, then, is merely for convenience.

Comparison No. 2: In the solid state, ionic substances exist as a large aggregate of oppositely charged ions in a rigid lattice with each ion surrounded by four to twelve ions of opposite charge, depending on the type of crystal lattice formed. Therefore, when the solid melts, in order to break up the ionic cluster to produce the ionic mobility of the liquid state, the coulombic attraction between many ions must be overcome. This requires considerable energy and prevents the salt from melting until high temperatures have been reached. Naturally, much higher temperatures, i.e., more heat energy, must be provided to separate the ions further for vaporization. Consequently, the boiling points of salts are extremely high, provided they can be reached without decomposition.

On the other hand, covalent bonds do not give rise to the large charges found in ionic substances. The covalently bonded molecules are essentially neutral. This causes only weak intermolecular forces and therefore requires relatively little energy to separate them. Consequently, the processes of melting, vaporization, and sublimation of covalent compounds require much smaller magnitudes of energy than for ionic substances; accordingly, the melting points and boiling points of covalent compounds are in much lower temperature ranges. This is illustrated by the series of chlorides shown in Table 1.3.

TABLE 1.3. MELTING AND BOILING POINTS OF A SERIES OF CHLORIDES

	Ionic		*Covalent*	
	$NaCl$	$MgCl_2$	BCl_3	CCl_4
Melting point	804°	712°	−107°	−23°
Boiling point	1413°	1412°	12.5°	76.8°

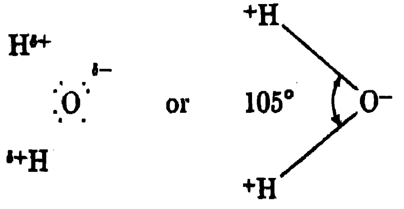
Most of the salts and solid inorganic substances encountered in general chemistry melt *above* 250° and boil *above* 750° if they boil before decomposition. In contrast to this, most organic substances melt *below* 250°, and generally those which boil without decomposition do so *below* 350°. The common organic substances already familiar to the student are liquids even at room temperature—alcohol, gasoline, ether, carbon tetrachloride, chloroform, kerosene—and this means that their melting points are below room temperature.

Comparison No. 3: Some molecules have high polarizabilities. That is to say, when they are brought near an electric charge, the negative particles within them (the electrons) are easily displaced from their normal positions (repelled by a negative charge and attracted by a positive charge). This tends to make one end of a molecule negative and one end positive, although the molecule is neutral as a whole. A body with a negative and a positive end is called a *dipole*, and if the dipole arises only when the molecule is brought near an electric charge, the dipole is said to have been *induced* by the electric charge. It is logical that the magnitudes of induced dipoles are proportional to the polarizabilities of molecules. In addition, within some molecules, the distribution of electrons and nuclei may cause the molecules to have permanent negative and positive ends. These molecules are always dipoles and are referred to as *polar molecules*. For example, in iodine monochloride, chlorine has the greater electronegativity, i.e., attraction for electrons, so that the shared pair of electrons is closer to, or spends more of the time traveling about, chlorine than iodine. This builds up the negative charge about the chlorine and decreases it about the iodine to create *formal charges* on the atoms (sometimes designated by $\delta-$ and $\delta+$ symbols) and makes the molecule a permanent dipole. The three degrees of polar character are exemplified by the chlorine compounds, molecular chlorine, iodine monochloride, and sodium chloride.

$Cl—Cl$	$^{\delta+}I—Cl^{\delta-}$	Na^+Cl^-
Nonpolar	Polar	Ionic

It should be pointed out here that even nonpolar molecules have small affinities for one another. The rapid oscillations of electrons about atomic nuclei create momentary alternating dipoles which will cause weak attractions between nonbonded atoms when brought close to each other. These forces are called *van der Waals forces* and operate only within short ranges. Hence, nonpolar molecules have extremely weak attractive forces between them (van der Waals forces); polar covalent molecules have stronger coulombic, but still relatively weak attractive forces between them; and ion pairs have large coulombic attractive forces between them. The melting and boiling points of these three types of compounds increase in this order owing to the increasing intermolecular attraction.

In water, for another example, the oxygen atom has the greater electronegativity and pulls the shared electron pairs toward itself and away from the hydrogen atoms. Formal charges arise on the atoms to make the oxygen end of the molecule the negative end, and the molecule is a permanent dipole.



When polar molecules have large polarizabilities, they make good solvents for ionic substances.[1] Such is the case for water, liquid ammonia, and sulfuric acid. When an ionic substance is placed in one of these polar solvents, the ions attract the polar solvent molecules. The negative ends of the polar molecules are bound to the cations and the positive ends to the anions. This weakens the interionic forces and eventually the two ions separate, being surrounded completely by solvent molecules.

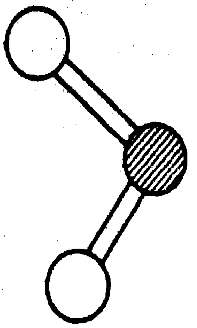
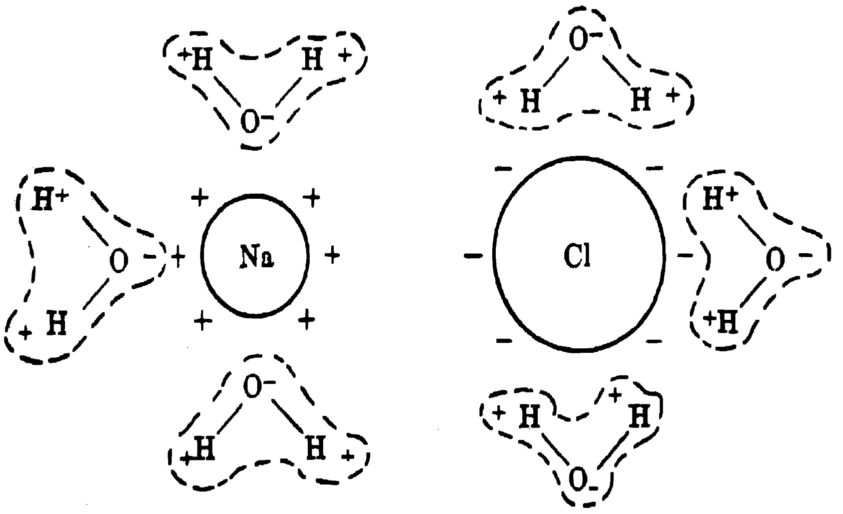


Fig. 1.9. Ball-and-stick model of the water molecule.

Diagrammatic sketch of the dissolution of a salt[2]



Salt is placed in water

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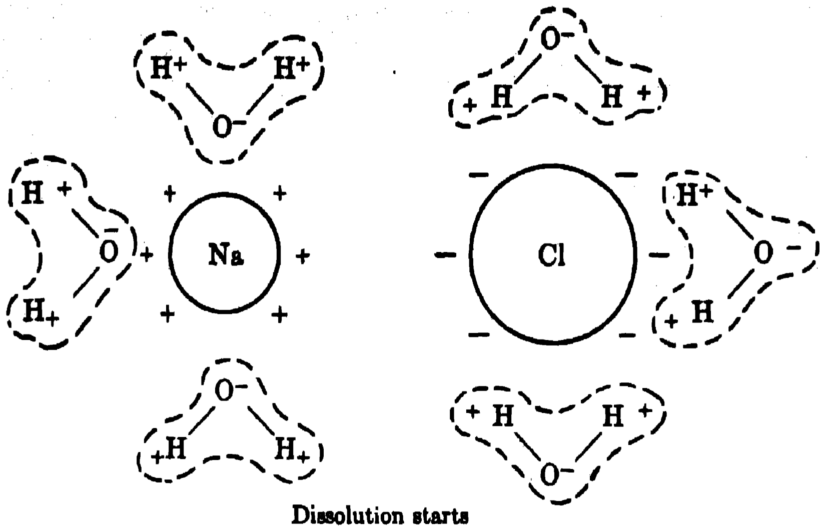
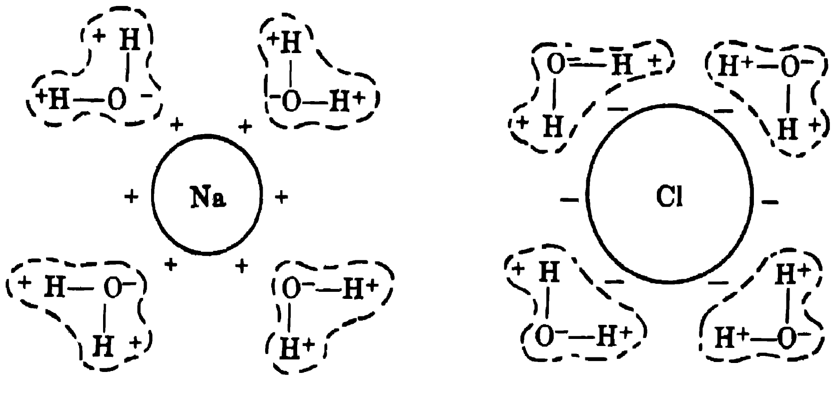
[1] Since the molecules of H_2O are polar, with large polarizabilities, the substance water has a large *dielectric constant.*

[2] The + and − signs represent only fractional charges.



Dissolution starts



Each ion is surrounded by water molecules (hydrated) and moves independently in the solution

This is a very oversimplified picture of the process of dissolution of salts. Actually there are so many factors which affect the solubility of a salt that there is no simple, generally applicable theory for the solubility of electrolytes. The most important factors are related to sizes and charges of the individual ions, and salt solubilities depend primarily upon how these factors determine the stability of the crystal and secondly upon how the solvent molecules weaken the crystal forces and stabilize the ions in solution. These various effects are summarized in Table 1.4.

Rarely does a covalent substance have a high dielectric constant, hence ionic substances normally do not dissolve to any appreciable extent in organic liquids. As a rule, inorganic substances dissolve only in liquids of high dielectric constants and usually then with ionization. In contrast to this, organic

TABLE 1.4. FACTORS INFLUENCING THE SOLUBILITY OF SALTS IN POLAR SOLVENTS*

Solubility Increased by (Stabilization of ion):	Solubility Decreased by (Stabilization of crystal):
1. Solvation of ions through coulombic attraction	1. Covalent bonding
2. Solvation of ions through covalent bonding (complexes)	2. High ionic charge densities
	3. Radius ratio near 0.75
	4. Ionic ratio of 1:1
	5. Hydrogen bonding in crystal
	6. Symmetrical ions
	7. Low temperatures

* L. E. Steiner and J. A. Campbell, *General Chemistry*, The Macmillan Company, New York, 1955, Chap. 24.

compounds do not tend to dissolve in water or liquids of high dielectric constants. Since polar molecules are attracted to one another, in the liquid state they consist of large clusters of associated molecules. Nonpolar solute molecules are unable to break up these clusters and therefore do not dissolve in the polar solvent to any appreciable extent. The forces of attraction between covalent molecules are relatively weak, and when an organic substance is placed in an organic liquid, the solute and solvent molecules show little preference in association and readily mix with each other. Hence, dissolution takes place, for it is nothing more than the intermingling of different molecules. This tendency for ionic substances to dissolve in polar but not in nonpolar solvents, and conversely, of nonpolar substances to dissolve in nonpolar but not in polar solvents, has led to the "rule of thumb" that *like dissolves like*. Nevertheless, when organic substances do dissolve, ions are not produced.

Comparison No. 4: It has been shown that inorganic substances ionize when they dissolve, and of course, moving ions may conduct a current. Too, when ionic substances melt, the ions gain freedom to move about independently. Therefore, molten ionic substances and solutions of ionic substances conduct electric currents. Since covalent compounds melt or dissolve without producing ions, their melts and solutions are nonconducting.

Comparison No. 5: Everyone knows that gasoline, kerosene, ether, and other common organic chemicals burn very readily; indeed, oils have long been used for domestic heating. The high flammability of organic chemicals is the chief concern of chemists in the laboratory. Care must always be taken to minimize the risk, and precautions must be taken to meet an emergency should an accident occur. On the other hand, inorganic substances rarely undergo combustion and therefore they do not present a hazard from the standpoint of laboratory fires.

In general, covalent compounds will readily undergo combustion, many spontaneously, so that most organic compounds will burn. As an exception, the polyhalogenated compounds, such as carbon tetrachloride, do so with difficulty. The difference in behavior of organic and inorganic compounds toward heat is the basis of a qualitative method of distinguishing the two. When a small sample of an unknown is gently heated on a spatula over an open flame, organic substances will either ignite and burn, volatilize, or melt and decompose to a charred residue. Inorganic substances will, in general, undergo no apparent change, although occasionally if the temperature gets high enough, they may be dehydrated and exhibit a change in color or crystalline form. Nevertheless, as a simple, quick method, this test is frequently used to determine whether a substance is organic or inorganic. When there is doubt after using this test, more reliable and more elaborate tests may be employed.

Comparison No. 6: Most inorganic reactions involve ions among the reacting species, and therefore take place in aqueous media. Consequently, the reactants are in the state in which they will react, and this allows the reaction to take place very rapidly when the reagents are mixed. That is to say, inorganic reactions are usually ionic and rapid. For instance, when aqueous solutions of sodium chloride and silver nitrate are mixed,

$$\underset{\substack{\text{in one}\\\text{vessel}}}{(Na^+ + Cl^-)} + \underset{\substack{\text{in second}\\\text{vessel}}}{(Ag^+ + NO_3^-)} \rightarrow Na^+ + NO_3^- + \underset{\substack{\text{a pre-}\\\text{cipitate}}}{AgCl}$$

the silver chloride precipitates immediately. Furthermore, inorganic substances normally react to give only one set of products. For example, a typical reaction like $2H^+ + 2Cl^- + Zn \rightarrow H_2 + ZnCl_2$ always involves these same substances irrespective of the molar ratio of reactants, the temperature, the order of mixing, or other experimental variations. Of course, not all reactions are as insensitive to changes in experimental conditions, but generally variations in experimental conditions do not cause large alterations in the types of products produced in inorganic reactions.

Organic reactions are, first of all, *molecular*. By that is meant that *molecules rather than ions react*. Secondly, in order for the reactants to give the products, chemical bonds within the reacting molecules must first be broken. This fission of covalent bonds may come about in several ways, three of which will be described here. First of all, a covalent bond consists of a shared pair of electrons. When the bond is broken, the electrons may be equally distributed, ***homolytic cleavage***, or both electrons may stay with one atom, ***heterolytic cleavage***.

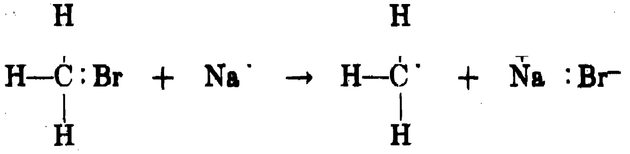
Homolytic Cleavage

$$A{:}B \rightarrow \underbrace{A^{\cdot} + B^{\cdot}}_{\text{Free radicals}}$$

Heterolytic Cleavage

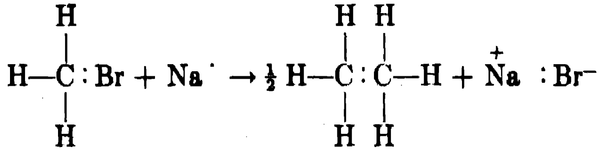
$$A{:}B \rightarrow \underset{\substack{\text{An}\\\text{anion}}}{A{:}^-} + \underset{\substack{\text{A}\\\text{cation}}}{B^+}$$

Homolytic fission produces two *free radical* fragments and is normally initiated by other free radicals or radiation. Heterolytic fission produces two ions and is usually initiated by ionic or polar reagents. Hence, it is called a *polar mechanism*. For example, sodium metal reacts with methyl bromide in solution to produce sodium bromide and a methyl radical.



$$H-\overset{H}{\underset{H}{C}}:Br + Na^{\cdot} \rightarrow H-\overset{H}{\underset{H}{C}}{}^{\cdot} + \overset{+}{Na}\ :Br^{-} \qquad (1)$$

The methyl radical is very reactive and two quickly combine to form ethane.[3] The net reaction is then,



$$H-\overset{H}{\underset{H}{C}}:Br + Na^{\cdot} \rightarrow \tfrac{1}{2}\,H-\overset{H}{\underset{H}{C}}:\overset{H}{\underset{H}{C}}-H + \overset{+}{Na}\ :Br^{-} \qquad (2)$$

An equally plausible mechanism for this reaction is the following:

$$R-X + Na^{\cdot} \rightarrow R^{\cdot} + Na^{+}X^{-}$$

$$R^{\cdot} + Na^{\cdot} \rightarrow {}^{-}R:Na^{+}$$

$${}^{-}R:Na^{+} + R-X \rightarrow R:R + {}^{+}NaX^{-}$$

That is, the alkyl free radical and a sodium atom form an ion-pair. The negative ion in this ion-pair, a *carbanion* in this case, attacks an alkyl halide molecule to *displace* the halogen atom. Not enough is known about the reaction to decide between these two proposed mechanisms for the reaction.

In a different case, aluminum bromide reacts reversibly with methyl bromide by the heterolytic process.

$$CH_3-Br + AlBr_3 \rightleftharpoons H_3C^{+} + {}^{-}AlBr_4 \qquad (3)$$

If benzene is present, the methyl cation (a *carbonium* ion) will attack it and produce toluene.

$$C_6H_6 + H_3C^{+} \rightarrow C_6H_5-CH_3 + H^{+} \qquad (4)$$

The overall reaction is then

$$C_6H_6 + CH_3Br + AlBr_3 \rightarrow C_6H_5-CH_3 + HBr:AlBr_3 \qquad (5)$$

Often the polar mechanism takes place without the temporary formation of ions. For instance, hydroxide ion reacts with methyl bromide by attacking the molecule from the side opposite to the bromine atom.

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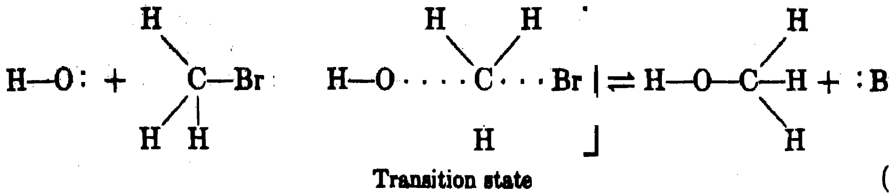
[3] The methyl radicals can react with one another only when a third body is present to absorb the excess energy or when the excess energy is emitted as heat.



(6)

As the hydroxide ion approaches the carbon atom and begins to form a bond, i.e., share an electron pair, the carbon-bromine bond becomes weaker and finally a stage is reached where carbon is weakly bonded to the oxygen and bromine atoms. This transitory stage is called a transition state and is conventionally written in brackets. At this point, the reaction may go forward to produce the products or go in the reverse direction to yield the original reactants. Much more will be said about these reactions later. They are given here merely to illustrate some of the mechanisms by which organic molecules react. As a generality, the polar and free radical mechanisms can be compared as follows:

Polar Reactions

1. Usually occur in solution or on polar surfaces but rarely in the gas phase.
2. Are often catalyzed by acids or bases, and their rates are strongly influenced by the polarity of the solvent.
3. Are seldom chain reactions (defined below).
4. Are rarely affected by radiation or reagents containing unpaired electrons, such as oxygen or decomposed peroxides.

Free Radical Reactions

1. Frequently occur in the gas phase, proceed by chain mechanisms, and often show induction periods.
2. Usually initiated by radiation, heat, or other free radicals.
3. Are inhibited by substances which readily react with free radicals.
4. Are rarely acid- or base-catalyzed, and their rates are usually independent of the polarity of the medium.

The detailed, step-by-step description of a chemical reaction is called a *reaction mechanism*. However, it is only a hypothesis proposed to account for the observations. The critical intermediate stage through which a reactant must pass to reach the product, called the *transition state* or *activated complex*, is not isolable; therefore one cannot say a reaction mechanism is proved. The more facts it accounts for and the more predictions that can be made based on the mechanism, the better established and the more confidence we have in the theory of organic chemistry. In this way, reaction mechanisms facilitate an understanding and the control of organic reactions, and eventually it might be possible for a chemist to synthesize any desired molecule.

The mechanisms of most reactions can be considered as substitution, addition, or elimination reactions, or combinations of these three types. The features of these three modes of reactions, therefore, will be presented in appropriate places in this book.

In our comparison of reactions of ionic and covalent compounds, we have just seen that the covalent molecules generally do not react as rapidly as the ionic substances because the covalent compounds must undergo some type of transition in order to pass from the reactant to the product. The organic reactions are also more complex than ionic reactions. Consider the reaction between bromine and methane.

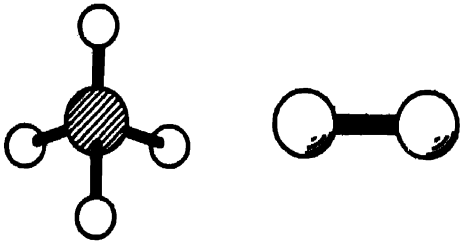
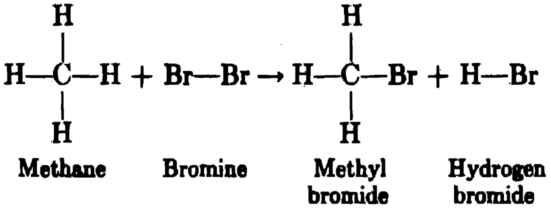


Fig. 1.10. Ball-and-stick models of the methane and bromine molecules.



$$\mathrm{H{-}\overset{\displaystyle H}{\underset{\displaystyle H}{C}}{-}H + Br{-}Br \rightarrow H{-}\overset{\displaystyle H}{\underset{\displaystyle H}{C}}{-}Br + H{-}Br} \qquad (7)$$

Methane Bromine Methyl bromide Hydrogen bromide

Before the reaction can take place, the bromine-bromine bond must be broken to yield two bromine atoms. This cleavage is effected by heat, by a metallic catalyst, or by radiation (in the last case, the process is called photodissociation and is normally brought about by sunlight, a 300–500-watt lamp, or an ultraviolet lamp). A bromine atom then abstracts a hydrogen atom from methane to form H—Br and a methyl free radical. The latter then attacks a bromine molecule to give a methyl bromide, and the bromine atom so liberated continues the cycle. This sequence of steps can be described by the following equations:

$$\mathrm{Br:Br \xrightarrow[\text{heat energy}]{\text{light or}} 2Br^{\cdot}} \qquad (8)$$

$$\mathrm{CH_4 + Br^{\cdot} \rightarrow H_3C^{\cdot} + H:Br} \qquad (9)$$

$$\mathrm{Br:Br + H_3C^{\cdot} \rightarrow H_3C:Br + Br^{\cdot}} \qquad (10)$$

When the bromine atom formed in equation (10) reacts with another methane molecule as in equation (9), it regenerates a methyl radical which may react with another bromine molecule as in equation (10). By repetition of reactions (9) and (10) the process of bromination is *propagated* without additional absorption of energy as needed in the initiation step (equation (8)). Such self-perpetuating reactions are called *chain reactions* and are terminated by any of several ways in which the formation of free radicals ceases.

The situation is even more complex because after an appreciable number of methyl bromide molecules have been produced in the reaction above, a bromine atom has a good chance of encountering and reacting with a methyl bromide molecule instead of with a methane molecule. Accordingly, the reactions

$$Br^{\cdot} + CH_3Br \rightarrow {}^{\cdot}CH_2Br + HBr$$

$$^{\cdot}CH_2Br + Br_2 \rightarrow CH_2Br_2 + Br^{\cdot}$$

will proceed at a significant rate, resulting in a second organic product. Obviously, when the concentration of CH_2Br_2 builds up, it too may react to produce $CHBr_3$, and this in turn can yield some CBr_4. Therefore when bromine is allowed to react with methane, all these products are produced, CH_3Br, CH_2Br_2, $CHBr_3$, and CBr_4, the amounts of each decreasing in this order. Furthermore, one cannot prevent the formation of any one or more of these products. Not all organic reactions will yield so many products; but usually more than one product can be formed, and for this reason organic reactions are complex in comparison to inorganic reactions.

The fact that several products are produced is not the difficulty; it is that they are not produced in any fixed stoichiometric[4] ratio. The molar ratio of the various possible products from an organic reaction is usually dependent upon experimental conditions of temperature, molar ratio of reactants, type of catalyst used, concentrations of reactants, *p*H, etc. Therefore the experimental conditions that yield the optimum quantity of desired product must be learned from controlled experiments. Then, the ratio of the amount of the desired product actually obtained to the amount which is theoretically possible, according to the equation for the reaction, is referred to as the *per cent yield*. This is the point of major concern to all organic chemists. How efficient is the process? Seldom are organic reactions 100 per cent efficient, even if allowances are made for mechanical losses, such as material sticking to reaction vessels. On the other hand, close to 100 per cent efficiency is not uncommon for inorganic reactions.

Comparison No. 7: Naturally an exact figure cannot be given, but it is a fair guess that the number of inorganic substances actually prepared and isolated is less than 100,000. There are 103 known elements; thus, excluding carbon, these 100,000 inorganic substances can be said to have been produced from two or more of the 102 remaining elements. In contrast to this, the number of isolated and identified organic compounds is approximately 1,000,000, the majority of which come from just the ten elements, carbon, hydrogen, oxygen, nitrogen, phosphorus, sulfur, and the four halogens. The symbols can be arranged to read, S. P. COHN, X, (S. P. Cohn the tenth) where X represents the halogens as a group. Thus, from one-tenth as many elements, the organic compounds outnumber the inorganic compounds ten to one.

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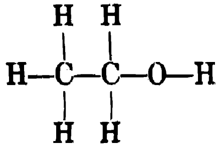
[4] The stoichiometric ratio of a reaction is the molar ratio of reactants and products indicated by the chemical equation for the reaction.

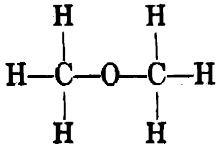
When atoms of like elements are joined together they do so through covalent bonds, and it is very rare to find atoms of like elements bonded together in inorganic substances. A few elements, however, particularly carbon, readily form long chains or rings of the same type of atoms. Therefore, several different organic molecules may contain the same number and type of atoms, but have different carbon skeletons. This gives rise to a phenomenon frequently found among covalent compounds, but not among ionic substances, namely, *isomerism*. Because of the formation of chains or rings of covalently bonded atoms, whereby several different molecules may have identical molecular formulas, covalent compounds outnumber ionic substances by a large ratio.

Comparison No. 8: *Isomers* are compounds having the same molecular formula but different molecular structures. Thus, two isomers contain identical types and atomic ratios of elements, but the atoms in the two isomers have different positions relative to one another in space. For example, ethyl alcohol and methyl ether may be represented by the graphic formulas:



$$\begin{array}{ccccccccc} & & H & & H & & & & \\ & & | & & | & & & & \\ H & — & C & — & C & — & O & — & H \\ & & | & & | & & & & \\ & & H & & H & & & & \end{array}$$

Ethyl alcohol



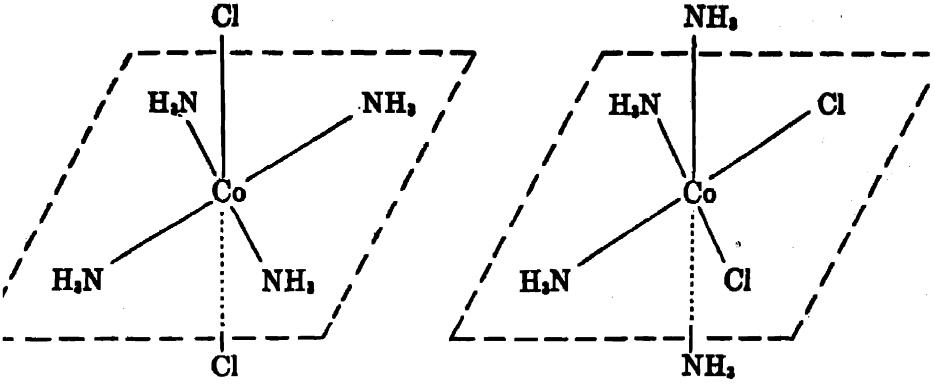
$$\begin{array}{ccccccccc} & & H & & & & H & & \\ & & | & & & & | & & \\ H & — & C & — & O & — & C & — & H \\ & & | & & & & | & & \\ & & H & & & & H & & \end{array}$$

Methyl ether

It can be seen clearly that in the alcohol molecule the oxygen atom is between a carbon and a hydrogen atom, and in the ether molecule the oxygen atom is located between two carbon atoms. Other differences can be seen, but one is sufficient to prevent the two molecules from being identical; and therefore they will have different properties. For instance, the alcohol readily reacts with sodium metal to liberate hydrogen but sodium does not react with the ether, and the alcohol is completely soluble in water whereas the ether is only moderately soluble in water.

Consequently the formula C_2H_6O may be given for ethyl alcohol as well as for methyl ether; hence, there must be a way of distinguishing the two compounds when using this chemical notation. In general then, molecular formulas are inadequate as a chemical shorthand when applied to organic compounds. Since isomers seldom occur among inorganic substances, molecular formulas can usually be employed to express inorganic chemical reactions.

Covalent bonds have definite, fixed directions in space about an atom and the resulting bond angles primarily determine the spatial arrangement of atoms within the molecule. For example, dichlorotetramine cobaltic chloride $(Co(NH_3)_4Cl_2)^+Cl^-$ can be prepared in a bright *green* isomer and a *violet* isomer whose structures differ in the arrangement of the covalently bonded ammonias and chlorine atoms about cobalt.



Green

Violet

On the other hand, ions exert electrostatic forces equally in all directions, forming ionic bonds in no preferred direction. Consequently, isomers do not arise. Isomerism, then, is not peculiar to organic compounds but to covalent compounds, and therefore occurs among covalent inorganic compounds as well. Since most inorganic substances are ionic, however, isomerism is not common among them. When it does occur, then diagrammatic structures must be employed, as is done for organic compounds.

It is noteworthy that an *empirical formula* for a compound indicates the *ratio* of the atoms of each element in a molecule of that compound and is found from an elemental analysis of the material. The *molecular formula* shows the *number* of atoms of each element in a molecule of the compound and is found from the elemental analysis plus a determination of the molecular weight of the compound. The experimental determination of empirical and molecular formulas was taken up in the course in general chemistry and could be reviewed at this time. In this connection, see Appendix A2 for assistance. A *graphic* or *structural* formula shows the type and *position* of all atoms in the compound and is obtained from the molecular formula plus certain knowledge about the physical and chemical properties of the compound.

For illustration, formaldehyde, acetic acid, lactic acid, and glucose all have the same chemical composition and hence have the same empirical formula, $(CH_2O)_n$. However, they have different molecular formulas: CH_2O, $C_2H_4O_2$, $C_3H_6O_3$ and $C_6H_{12}O_6$, respectively. This reveals the importance of determining molecular weights, and indeed organic chemists were quite frustrated until

Stanislao Cannizzaro in 1860 pointed out how simply the situation could be resolved if Amadeo Avogadro's hypothesis of 1811 were accepted.

In 1860 at the insistence of Wurtz, Kekulé, and one or two other prominent chemists, a convention was called at Karlsruhe in the hope of bringing some general understanding or formal compromise concerning the confusion on atomic weights and chemical notation. The convention proceeded with many brilliant speeches being made, but no general agreement was reached. At the close, Cannizzaro, a student of Avogadro, distributed a pamphlet describing how he taught theoretical chemistry based on Avogadro's hypothesis. The discrepancies, conflicts, and confusion of that period cleared up very quickly after the value of Avogadro's hypothesis was recognized.

In this section, the broad differences in characteristics between ionic and covalent substances have been discussed extensively. Because of this marked contrast in behavior between ionic and covalent substances, and the fact that there are so many compounds of carbon, it is conventional to study organic chemistry as a separate branch of chemistry. Whether or not this is the wisest procedure is a topic of current debate. This lengthy discussion here was not given as justification for studying the two classes of substances separately, but rather to get the student acquainted with some of the general characteristics of organic substances and to help him with the transition from ionic to covalent substances.

STUDY EXERCISES[7]

1. In a sentence or two, cite a contribution to chemistry made by each of the following named persons: G. N. Lewis, S. Cannizzaro.
2. What properties of stannic tetrachloride resemble those of carbon tetrachloride? What is one way in which the two compounds differ markedly?
3. What physical properties of an atom are related to its atomic number?
4. Why is water more likely to extinguish burning grain alcohol than burning gasoline?
5. Would you expect the organic compound C_3H_7Cl to give an immediate precipitate of silver chloride when treated with an aqueous solution of silver nitrate? Why or why not?
6. Why is it necessary to determine molecular weights of compounds?
7. State briefly several ways in which the properties of organic and inorganic substances differ and in what respects reactions of the two classes of substances differ.
8. Calculate the percentage composition of: (a) C_2H_6O; (b) C_2H_3OCl; and (c) $C_6H_7N_2ClSO_2$.
9. Quantitative analysis of an organic hydrocarbon gave the following results:

weight of sample....................	0.200 g.
weight of CO_2 produced.............	0.550 g.
weight of H_2O produced.............	0.447 g.

Calculate the empirical formula of the compound.

10. The freezing-point constant of camphor is 40. In a given experiment, 100 mg of camphor (melting point 178°) were mixed with 10 mg of *unknown*. The mixture melted at 170°. What was the molecular weight of the unknown compound?

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[7] For aid in the solution of mathematical problems, see the Appendix.

11. A gas has the following per cent composition: C, 81.8; H, 18.2. One liter at 0° and 760 mm pressure weighs 1.965 g. What is its molecular formula?

12. Why is it not surprising that a carbon-carbon bond is covalent rather than ionic?

13. What information is required to determine an empirical formula, a molecular formula, and the structural formula for an organic compound?

14. What is a polar molecule? Why is an alcohol a polar molecule?

15. If $BeCl_2$ is covalent, what type of bond orbitals does beryllium use in forming the Be—Cl bond?

16. Explain the fact that carbon can form only four covalent bonds as in CF_4 while silicon, right below carbon in the periodic table, can have a covalency of six as in the ion SiF_6^-.

17. If 17.2 mg of CH_2Cl_2 were heated in a bomb with sodium peroxide and the chloride precipitated as silver chloride, what weight of silver chloride would you expect?

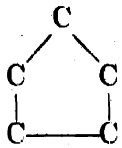
1.3 CLASSIFICATION AND SOURCES OF ORGANIC COMPOUNDS

Since there are so many organic substances, it is to be expected that there should be a well-organized system of classifying organic compounds, and this is true. First of all, they are divided into three broad groups:

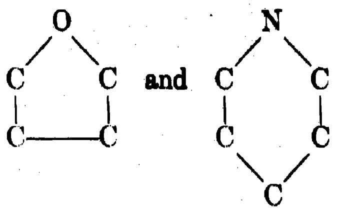
a. Aliphatic (Gr. *aleiphar*, fat) so named because fats are some of the most typical members: open-chain compounds in which the carbon atoms are linked in such a manner that no closed rings containing carbon are formed. The compounds may be *saturated*, in which carbon atoms form only single bonds, or they may be unsaturated, in which one or more carbon atoms form multiple bonds, i.e., double or triple covalent bonds.

b. Carbocyclic (sometimes *isocyclic* or *homocyclic*): compounds in which occur closed rings of carbon atoms only. There are two subdivisions of carbocyclic compounds: (a) *alicyclic* or *cycloaliphatic*, in which the closed-ring compounds resemble the aliphatic compounds in properties, including saturated and unsaturated members; (b) *aromatic* compounds, in which the closed-ring carbon atoms form multiple bonds but in spite of their unsaturation, do not behave like the unsaturated aliphatic or cycloaliphatic compounds.

c. Heterocyclic: compounds in which there is at least one ring containing one or more atoms of another element or elements, such as nitrogen, oxygen, or sulfur. This division includes all compounds containing at least one heteroring, whether saturated or unsaturated and whether they have aromatic character or not. However, the properties of a few heterocyclic compounds resemble so closely those of the aliphatic compounds, from which they are formed easily be a cyclization process and to which they readily revert by ring opening, that they are commonly discussed along with the aliphatic compounds.



Skeleton formula of an alicyclic compound



Skeleton formulas of heterocyclic compounds

Sources of organic chemicals. The principal natural resources for organic chemicals are plants and carbonaceous materials as shown in the chart in Figure 1.11. Although the major portion of organic chemicals comes from coal, natural gas, and petroleum, only about 2 per cent of these materials is used for chemical production; the remaining 98 per cent is consumed as fuel. New deposits of these materials have steadily been found, but now they are being consumed at a far greater rate than nature is producing them, and it is only a matter of time before the supply will be exhausted. Hence the quantities of these natural resources available for fuel, and secondly for chemicals, are of considerable interest to the nation. The country's energy reserves have been a topic of major concern in recent years. Congress, the National Science Foundation, and various organizations are sponsoring studies and pilot experiments to find a new cheap, abundant source of energy. The country's population is steadily increasing and energy needs grow at a faster rate than the population. The United States is consuming 10 per cent more raw materials than it is producing, whereas fifty years ago 15 per cent more raw materials were produced than consumed. The United States produces over half the world's supply of oil, but this is insufficient to meet even domestic needs and this country has shifted from one of the world's largest exporters of oil to one of the largest importers. Estimates show that the present conventional sources of energy may be exhausted for practical purposes in about 100 years. From what is known now, the alternative sources are nuclear and solar energy.

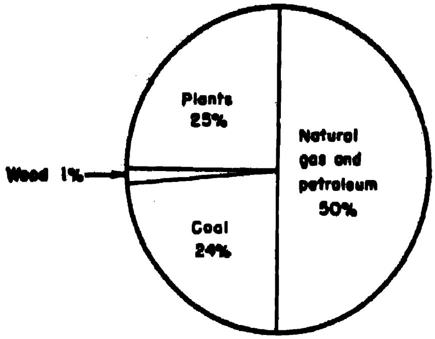


Fig. 1.11. Natural resources of organic chemicals.

It is to be realized that when solar energy does become commercially available, it does not mean that it will replace, but rather will supplement the present sources of power. When new devices and inventions are developed, seldom do they completely replace existing methods, but supplement the older methods. For example, television has not put the movies out of business, airplanes have not displaced trains, telephones have not stopped letter writing, and even candles have a place in the present electric-light age. So it is that solar batteries, solar engines, photosynthesis, and other conceivable methods of harnessing solar energy will not replace the present sources of energy, and it is doubtful that they will be used much in crowded cities. However, many uses of solar energy will be found in suburbs and rural areas, and it will be a big factor in the industrialization of underdeveloped areas and in preserving the supply of fossil fuels for chemical industries. This latter point is important because the flow of fossil fuel into industrial processes is markedly increasing. For instance, detergents from oil and coal are replacing soaps made from animal fats; synthetic rubber from oil has partially supplanted rubber from trees; nylon from coal or oil has made silk garments things of the past; modern transportation consumes vast amounts of oil; and most plastics stem from oil or coal. Progress is being made so rapidly on the utilization of solar energy that by the time this manuscript reaches print, what has been said here will probably be obsolete.

1.4 STRUCTURAL THEORY OF ORGANIC CHEMISTRY

The nineteenth century postulates of the Kekulé-Couper-Butlerov trio provided embryonic notions which grew into the structural theory of organic chemistry, according to which the properties of a compound are attributable to the types of atomic groupings present in that compound. Hence, substances were classified according to the types of groups or organic radicals occurring in their structures, and all those containing the same type of radical were considered of one class or family. A few of the common atomic groupings that have been recognized and their classification names are:

Alcohol	$—OH$	Ether	$C—O—C$
Aldehyde	$—CHO$	Ketone	$—CO—$
Acid	$—COOH$	Acid chloride	$—CO—Cl$
Amide	$—CONH_2$	Nitro	$—NO_2$
Amine	$—NH_2$	Sulfonic acid	$—SO_3H$

These atomic groupings are called *functional groups* because they are largely responsible for the properties exhibited by organic compounds. Compounds containing more than one functional group in their structures are called *polyfunctional compounds*, and usually exhibit all the properties characteristic of each of the functional groups present.

According to the structural theory, if one knows which functional groups are present in a given compound, and if the characteristic attributes of each of these functional groups are known, then one could predict the properties of the compound. This would mean that all the compounds having an OH group in them would have certain properties in common, and so forth. This notion brought about a tremendous simplification in the chemistry of the thousands of organic compounds; and indeed elementary organic chemistry consists largely of learning the chemical and physical properties associated with the most common functional groups.

As more was learned about organic compounds, slowly it became apparent that the nearness of one functional group may affect another, and that the overt properties of a compound are the result of not only the types of functional groups present, but also of their relative positions to each other in that compound. So, modifications were made in the structural theory to recognize these *intergroup* effects, some of which are now known as *conjugation*, *tautomerism*, *resonance*, and *steric hindrance*. That means that the student will also have to learn what some of these intergroup effects are, when they occur, and how they alter the characteristics of the various functional groups.

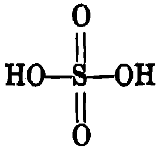
What is more, chemists are curious as to what factors are responsible for the observed properties exhibited by the various functional groups. That is, they want to know what basic forces contribute to the over-all observed behavior of substances. Such knowledge would help chemists to plan the structure of a compound which would have any desired chemical, physical, or biochemical property. The electronic theories of atoms, molecules, and chemical bonding have made possible considerable progress in this direction. In fact, the major difference between elementary and advanced organic chemistry is the extent to which the student attempts to interpret the behavior of substances in terms of electronic structures. Some of the electronic concepts are easy to understand and will facilitate an understanding of the intergroup effects. Therefore, a portion of the electronic theory of organic chemistry is taken up even at the elementary level.

Upon examination of the formulas of simple compounds, such as CH_4, CCl_4, $CHCl_3$, CH_3OH, $CH_3—O—CH_3$ and CH_3CH_2OH, it appeared to Kekulé that carbon must have a fixed covalence of 4, hydrogen a valence of 1, and oxygen 2. Then he reasoned that if the valence of carbon and hydrogen are to be the same in such well-known compounds as CH_4, C_2H_6, C_3H_8, and C_4H_{10}, then carbon atoms must form bonds with other carbon atoms. Later similar lines of thought revealed that the common covalences of other elements in neutral organic compounds are normally as shown in Table 1.5.

TABLE 1.5. COMMON COVALENCES

Normal covalence =	1	2	3	4	3	2	1
	H						
	Li	Be	B	C	N	O	F
			Al	Si	P	S	Cl
							Br
							I

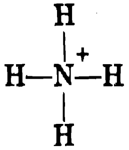
It is noticeable that these covalences are related to the positions of the elements in the periodic table. By using additional atomic orbitals, elements in the third row and below may have other covalences also, which will be learned later. For example, sulfur has a covalence of 6 in sulfuric acid, i.e., forms six covalent bonds.



$$\mathrm{HO{-}\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O}{\|}}{S}}{-}OH}$$

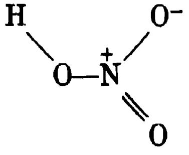
For the present, unless an exception is pointed out, it will be best to use only the covalences given in Table 1.5. Each time the student writes a structural formula, he should check to see if these covalency rules have been followed.

Owing to the basicity of nitrogen, after it has formed three covalent bonds it readily will donate its unshared pair of electrons to an acceptor atom to form a coordinate covalent bond. In so doing, it acquires a positive charge as in the ammonium ion.

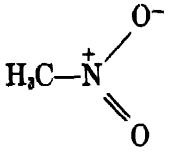


$$\mathrm{H{-}\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle H}{|}}{N}}{}^{+}{-}H}$$

Thus when nitrogen breaks the covalence rule of three, it will be charged. This is its condition in nitric acid and organic nitro compounds.



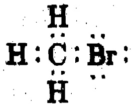
Nitric acid



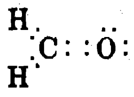
Nitromethane

Furthermore, Kekulé adduced that an atom may form multiple covalent bonds with another atom, i.e., a double or a triple covalent bond, provided the total number of covalent bonds formed obeys the covalence rules. Thus carbon may form four single bonds or two single bonds plus one double bond; nitrogen may form three single bonds or a triple bond. It is conventional to let dashes represent covalent bonds, so the various combinations can be sketched as shown in Table 1.6. The alternatives for oxygen of —O— or O= are illustrated in the compounds formaldoxime and formaldehyde; hydrogen and the halogens are monovalent. These formulas need not be memorized. They are given merely to illustrate the constancy in covalence, irrespective of whether only single, or single plus multiple bonds are formed.

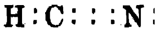
Since a covalent bond is a shared pair of electrons, the electronic structures of some of these compounds are:



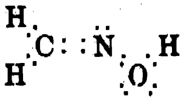
Methyl bromide



Formaldehyde



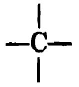
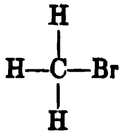
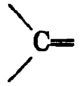
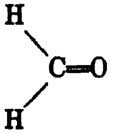
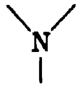
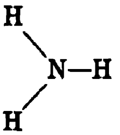
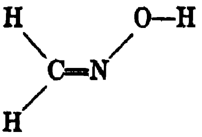
Hydrogen cyanide



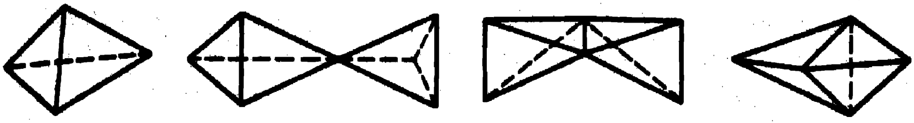
Formaldoxime

The structures of these same compounds may also be written as CH_3Br, H_2CO, HCN, and $H_2C{=}NOH$, and methyl ether as $H_3C—O—CH_3$. Such formulas are called *line formulas* and provide a convenient, concise chemical notation for use in text or equations. Hence there are several types of formulas

TABLE 1.6. BONDING VARIATIONS FOR CARBON AND NITROGEN

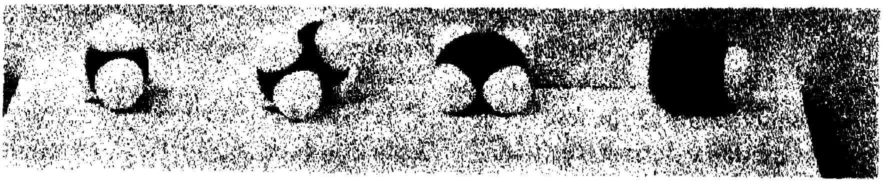
Element	Skeletal Structure	Specific Example	Name of Compound
Carbon			Methyl bromide
			Formaldehyde
	$—C\equiv$	$H—C\equiv N$	Hydrogen cyanide
Nitrogen			Ammonia
	$—N=$		Formaldoxime
	$N\equiv$	$H—C\equiv N$	Hydrogen cyanide

which are used for chemical symbolism. These are the structural or graphic formulas, the line formulas, and the electronic structures as given above. Naturally, the one that best expresses the point in question is employed. Moreover, sometimes written structures are inadequate to express certain three-dimensional relationships and molecular models must be used. Pictures of some molecular models are shown in Figure 1.12. The tetrahedral models



Tetrahedral models (above)

Brode and Boord ball-and-stick models (below)



Stuart-Briegleb molecular models (above)

Graphic or structural formulas (below)

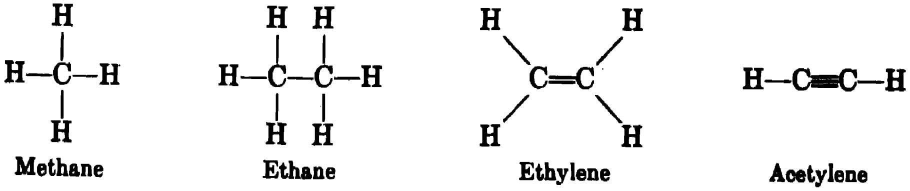


Fig. 1.12. Different representations of the molecules of methane, ethane, ethylene, and acetylene.

illustrate the spatial volumes formed by the carbon bonds. A tetrahedron is a symmetrical four-sided object, and any one of its four faces may be its base and any one of its corners the apex. Projection of the tetrahedral models onto a plane gives the corresponding two-dimensional projection formulas. The ball-and-stick models exaggerate interatomic distances, but these models are more clearly seen from a distance so that they serve best for classroom demonstrations. The Stuart-Briegleb models are built to scale with respect to atomic radii and bond angles. Obviously they are more revealing about actual molecular shapes and spatial requirements.

One strong supporting feature of the structural theory was its ability to account for the number of isomers observed for a given molecular formula. In the methane molecule CH_4, all four hydrogen atoms are equivalent. Indirectly this is believed to be so because isomers never have been isolated for any compound in which one hydrogen atom of methane has been substituted by some atom or group. Thus no matter under what conditions or who made CH_3Cl, CH_3NO_2, CH_3COOH, etc., no isomers have ever been isolated or detected for any of these substances. Direct evidence for the equivalency of the 4 hydrogen atoms in CH_4, that is, of the four carbon valences, was obtained by Henry as shown on page 432.

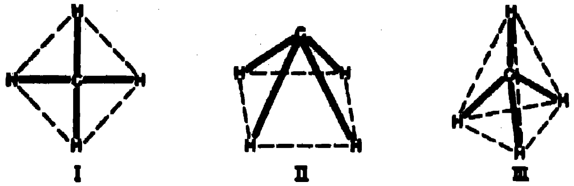


Fig. 1.13. Possible atomic arrangements of methane.

The equivalency of the four valences of carbon restricts the atomic arrangement of methane derivatives to one of three shapes: a planar (I), a pyramidal (II), or a tetrahedral (III) configuration (Figures 1.13 and 1.14). However, failure to isolate or even to detect the presence of isomers of disubstituted products of methane, CH_2X_2, eliminates the planar and pyramidal structures; for with structures I or II, two isomers would be possible, depending on whether the two substituents held opposite or adjacent positions, i.e., IV or V. The student should convince himself with models that no matter which two hydrogen atoms of methane are replaced by two substituents, only one type of molecule can be produced on the basis of a tetrahedral carbon atom.

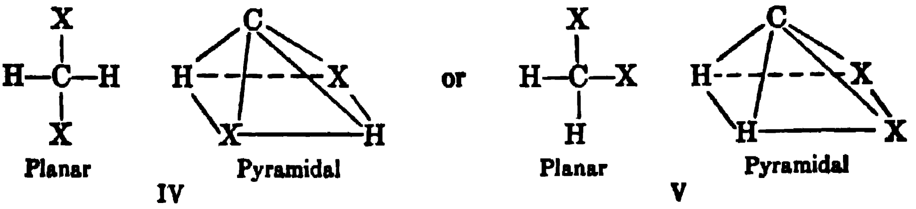


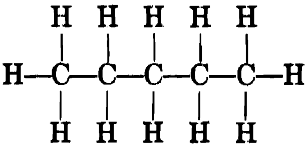
Fig. 1.14. Conceivable atomic arrangements of methane derivatives.

1.5 NOMENCLATURE

In organic chemistry it is necessary to have a system not only suitable for classification and organization but also adequate for naming the hundreds of thousands of organic compounds. Whatever system is adopted, it should provide a unique, unambiguous name for each compound. Aware of this fact, an international commission of chemists met in Geneva, Switzerland, in 1892 and adopted a system of nomenclature. This system was supplemented by the International Union of Chemistry, and is interchangeably referred to as the Geneva system, or the I.U.C. system of nomenclature.

Very often when new compounds of special interest are produced they are given *trivial* names for convenience. For example, acetone, stearic acid, cortisone, nylon, and many others are tremendously more simple than their correct chemical names. These trivial names have little relation to their structures, and most often are catchy names or terms which are adopted by persons using the substances frequently. Usually they fall into common use in preference to the longer systematic I.U.C. names and for this reason the student must become familiar with them. The most frequently encountered *trivial* or *common* names will be given as the compounds are taken up in this book.

Before the Geneva system is taken up the names of a few simple organic groups will be discussed. The simplest organic compounds are those containing carbon and hydrogen only, called *hydrocarbons*. As Kekulé first proposed, the carbon atoms may be joined together to form chains of indefinite length. For five carbons, for example, this can be sketched as follows:



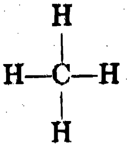
$$\begin{array}{ccccccccccccc} & & H & & H & & H & & H & & H & & \\ & & | & & | & & | & & | & & | & & \\ H & — & C & — & C & — & C & — & C & — & C & — & H \\ & & | & & | & & | & & | & & | & & \\ & & H & & H & & H & & H & & H & & \end{array}$$

The first class of aliphatic organic compounds to be studied will be the alkanes, and the structural features they have in common are (1) they contain carbon and hydrogen only, and (2) the carbon atoms form only single bonds. Their names are based on the number of carbon atoms in them, and the names for the first five members are methane, ethane, propane, butane, and pentane.

Many chemical terms are of Greek or Latin origin and it is preferable that compounded words be of pure Latin forms (as, *univalent* rather than *monovalent*) or of pure Greek forms (as, *monocyclic*). Some common Greek and Latin numerical prefixes are given here:

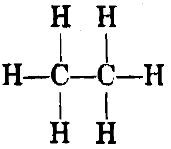
	Greek	*Latin*
½	hemi-	semi-
1	mono-	uni-
2	di-	bi-
3	tri-	tri-, ter-
4	tetra-	quadri-
5	penta-	quinque-
6	hexa-	sexi-
7	hepta-	septi-
8	octa-	octa-
9	ennea-	nona-
11	hendeca-	undeca-

The names of most hydrocarbons and related compounds are of Greek origin, althoug the Latin prefixes are used in favor of the Greek for *nine* and *eleven*.



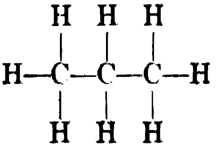
$$\begin{array}{c} \text{H} \\ | \\ \text{H—C—H} \\ | \\ \text{H} \end{array}$$

or CH_4 Methane



$$\begin{array}{c} \text{H}\;\;\text{H} \\ |\;\;\;\;| \\ \text{H—C—C—H} \\ |\;\;\;\;| \\ \text{H}\;\;\text{H} \end{array}$$

or $CH_3—CH_3$ Ethane



$$\begin{array}{c} \text{H}\;\;\text{H}\;\;\text{H} \\ |\;\;\;\;|\;\;\;\;| \\ \text{H—C—C—C—H} \\ |\;\;\;\;|\;\;\;\;| \\ \text{H}\;\;\text{H}\;\;\text{H} \end{array}$$

or $CH_3—CH_2—CH_3$ Propane

For butane, one can write $CH_3—CH_2—CH_2—CH_3$ or $CH_3—(CH_2)_2—CH_3$, and for pentane, $CH_3—CH_2—CH_2—CH_2—CH_3$ or $CH_3—(CH_2)_3—CH_3$. When an alkane has lost a hydrogen atom the residue is called an *alkyl group*, whose specific name is based on that of the original alkane with *-ane* changed to *-yl*. For instance, there are the groups, methyl (often abbreviated "Me") $—CH_3$, ethyl (sometimes abbreviated "Et") $—CH_2—CH_3$, propyl $—CH_2—CH_2—CH_3$, and so on. In the past it was customary to refer to these groups as radicals, but in the last 30 years, the term *free radical* has become known conventionally to mean a *free group* which has an unpaired electron. The term *group* connotes merely a portion of a molecule that remains unchanged as the molecule goes through a given reaction. On the other hand, a *functional group* is an atomic aggregate which is responsible for some of the characteristic chemical and physical properties of a molecule and generally undergoes the same reactions whether in a small or large molecule.

Fig. 1.15. Ethane, and orientations of the ethyl group.

It is noteworthy that only one methyl radical is possible. That is, irrespective of which of the four hydrogen atoms of CH_4 is removed, only one $CH_3—$ group results. Similarly, ethane has six equivalent hydrogen atoms. This is

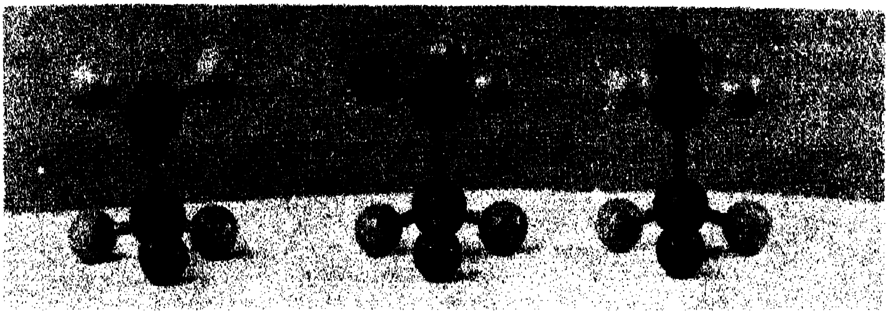


Fig. 1.16. Ball-and-stick models of *cis, gauche,* and *trans* conformations of 1,2-dichloroethane.

so, because first, the two methyl groups of ethane are equivalent. It makes no difference from which end a hydrogen atom is removed to give CH_3—CH_2— or —CH_2—CH_3; the two groups are indistinguishable. Second, the three hydrogens of either methyl group of ethane are equivalent because of *free rotation* about the C—C bond. That is, the three orientations of the ethyl group which would result by removing different H's from the particular —CH_3 group are indistinguishable because rotation about the C—C bond takes place easily to transform any one form into the others. By merely rotating the CH_2— group about the C—C bond, all three forms will fit into the same mold. Because of this free rotation about a C—C bond, only one isomer of symmetrical dichloroethane, Cl—CH_2CH_2—Cl, can be isolated. Three configurations are theoretically possible, referred to as the *cis, gauche,* and *trans conformations* (Figure 1.16). Looking along the C—C axis of the dichloroethane molecules, they appear as illustrated in Figure 1.18.

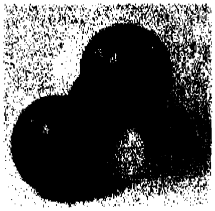
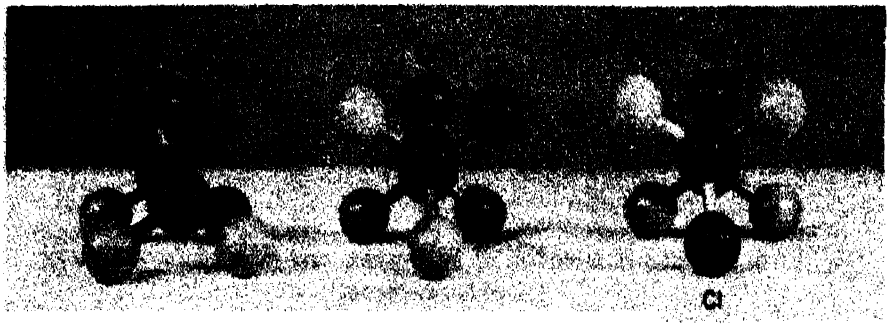


Fig. 1.17. Stuart-Briegleb molecular model of 1,2-dibromethane, showing contact of non-bonded bromine atoms in *cis* conformation.

In the *cis* conformation, the two C—Cl bonds are parallel, in the *trans* they are antiparallel, and in the *gauche* conformation one CH_2Cl group is rotated 60° about the C—C bond away from the *cis* position. These different configurations are referred to as *conformations,* i.e., different configurations of a molecule which differ from one another by a rotation of two groups about a single bond. It requires little energy to bring about the rotations in dichloroethane: merely that amount which may arise from the exchange of energy in a collision of two molecules at room temperature. Therefore, a mixture of such conformations cannot be resolved. By advanced techniques chemists can get evidence of their presence, but are unable to get a sample of material containing only one type of conformation. Because of the ease of rotation about single bonds, it is commonly spoken of as *free rotation*, although it is now known that small amounts of energy are required to bring about such rotations.

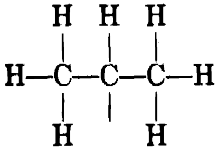


cis *gauche* *trans*

Fig. 1.18. Conformations of dichloroethane.

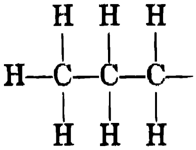
Since there is only one methyl group, the molecular formula $-CH_3$ can be used unambiguously to refer to this group. Similarly, there is only one group with the molecular formula $-C_2H_5$ (ethyl) and only one compound with the formula C_2H_6 (ethane), so that molecular formulas are sufficient to indicate these substances. On the other hand, isomerism exists for all other alkyl groups, making molecular formulas inadequate for representing these groups.

When a hydrogen atom is removed from propane, two distinguishable structures may result:



$$\begin{array}{ccccccc} & H & & H & & H & \\ & | & & | & & | & \\ H- & C & - & C & - & C & -H \\ & | & & | & & | & \\ & H & & & & H & \end{array}$$

and



$$\begin{array}{cccccc} & H & & H & & H \\ & | & & | & & | \\ H- & C & - & C & - & C- \\ & | & & | & & | \\ & H & & H & & H \end{array}$$

Therefore, there must be a method of referring to each particular propyl group. The one on the right is called *normal propyl* or *n*-propyl, because a straight chain of carbon atoms is conventionally called a *normal chain*. When this propyl group is attached to an atom or a portion of a molecule, its carbon atoms extend out in a straight chain. The group on the left is called the *isopropyl group*. The prefix *iso-* means that a chain of carbon atoms is branched at the end like a fork ——<, each prong being one carbon atom only in length.[8] If there are five carbon atoms in a group, the forked chain is called *isopentyl*.

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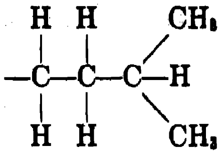
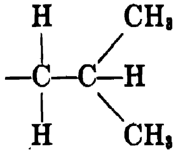
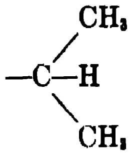
[8] The chemical use of the prefix *iso-* seems to have originated with Berzelius in 1832. In its broad sense it means simply "an isomer of." In aliphatic chemistry it has come to



If there are four carbon atoms, it is called *isobutyl.*



And if there are three carbon atoms, it is called *isopropyl.*



Thus, the isopropyl group is the smallest possible iso- group.

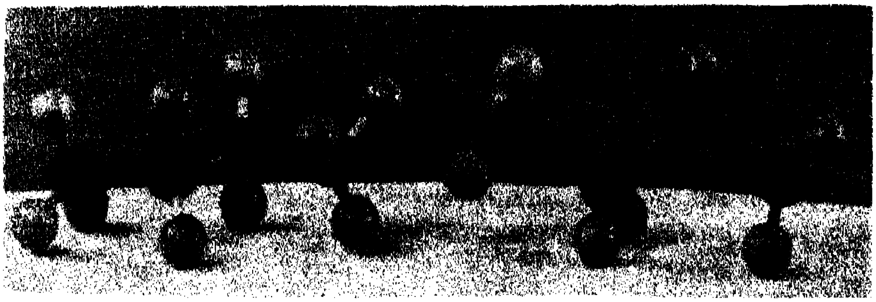


Fig. 1.19. Ball-and-stick models of the butane molecule from two views at right angles to each other.

The student must realize also that structural formulas are merely projections of models onto a plane. For example, two different views of a ball-and-

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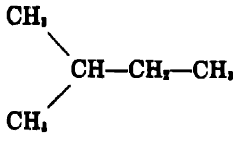
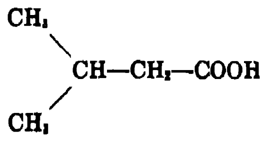
have a special meaning of an isomer characterized by the group $(CH_3)_2CH—$ attached to an otherwise straight chain, as in isopentane and isovaleric acid.



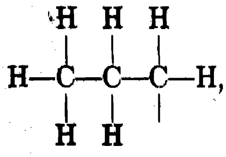
Isopentane



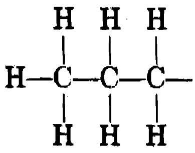
Isovaleric acid

It has, however, been difficult to maintain this distinction; for example, Isooctane, the high-octane gasoline, does not have this structure (page 78). In consequence, the International Union has restricted the special sense to chains of six or fewer carbon atoms; isohexyl, $(CH_3)_2CH—CH_2—CH_2—CH_2—$ is the longest radical of this kind recognized.

stick model of the butane molecule are shown in Figure 1.19. Notice, too, that the structural formulas of the *n*-propyl group,

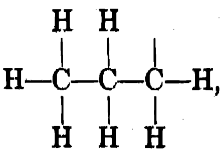


$$\begin{array}{ccccccccc} & & H & & H & & H & & \\ & & | & & | & & | & & \\ H & - & C & - & C & - & C & - & H, \\ & & | & & | & & | & & \\ & & H & & H & & & & \end{array}$$



$$\begin{array}{cccccccc} & & H & & H & & H & \\ & & | & & | & & | & \\ H & - & C & - & C & - & C & - \\ & & | & & | & & | & \\ & & H & & H & & H & \end{array}$$

and



$$\begin{array}{ccccccccc} & & H & & H & & & & \\ & & | & & | & & | & & \\ H & - & C & - & C & - & C & - & H, \\ & & | & & | & & | & & \\ & & H & & H & & H & & \end{array}$$

are equivalent, and differ merely by the angle of rotation of the $—CH_2$ group about the C—C bond. This is most clearly apparent when models are used, such as those shown in Figure 1.20.

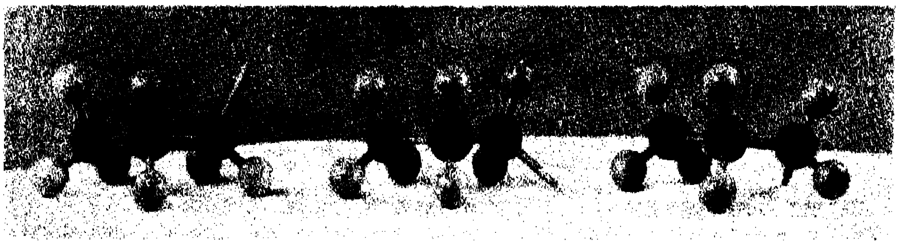
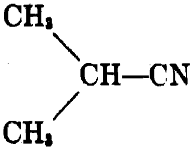


Fig. 1.20. Ball-and-stick models of the *n*-propyl group.

When a simple atom or group is attached to these alkyl groups at the carbon which has the open valence, the resulting compound is named by adding the name of the attached atom or group to that of the name of the alkyl group. The following examples are given for illustration:

$CH_3—CH_2—Cl$	Ethyl chloride
	Isopropyl cyanide (—CN is the cyanide group)
$CH_3—CH_2—CH_2—Br$	*n*-Propyl bromide
CH_3OH	Methyl alcohol (compounds containing an OH group are called *alcohols*)

Before considering the butyl groups, there is one detail to be taken up. A carbon atom having only 1 other carbon atom attached to it is referred to as a *primary carbon atom;* one having two other carbon atoms attached to it is a *secondary carbon atom;* one having three other carbon atoms attached to it is a *tertiary carbon atom,* and one having four other carbon atoms attached to it is a *neo*[9] *carbon atom.* Such carbon atoms are pointed out in the structure below.

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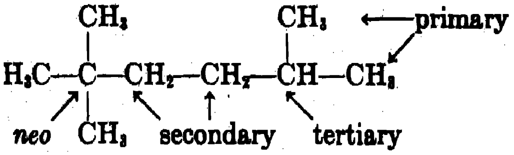
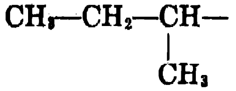
[9] The term *neo* arose from the fact that of the three isomeric pentanes, the last to be discovered was $(CH_3)_4C$ and was called *neopentane* (*neo-* for new).



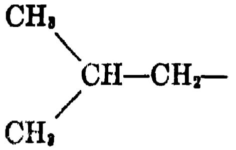
The butyl groups may now be discussed; they are as follows:

$CH_3-CH_2-CH_2-CH_2-$ *n*-Butyl group

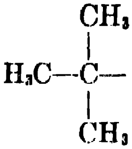


$CH_3-CH_2-\underset{\displaystyle CH_3}{\underset{|}{C}}H-$

Secondary-butyl group
(*sec.*-butyl or *s*-butyl)



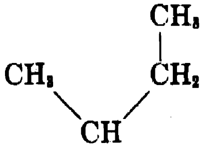
Isobutyl group
(*i*-butyl)



$H_3C-\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle CH_3}{\overset{|}{C}}}}-$

Tertiary-butyl group
(*tert.*-butyl or *t*-butyl)

It can be observed that there are two types of carbon skeletons here. For the straight chain of carbon atoms, there are two different butyl groups. The name *sec*-butyl is used to indicate that the straight chain is to be attached by one of the secondary carbon atoms, either one giving rise to the same butyl group. Thus, the two secondary carbon atoms in *n*-butane are equivalent and a hydrogen atom removed from either one produces the same *sec*-butyl group; i.e., $CH_3-\overset{|}{C}H-CH_2-CH_3$ is identical to $CH_3-CH_2-\overset{|}{C}H-CH_3$, but the two are oriented differently in space. The two models can be turned around in space to occupy identical volumes, or in different words, they would fit the same mold. This is referred to as being *spatially identical.* At the same time, because of free rotation, the *sec*-butyl group may have another conformation such as



where the ethyl group has rotated about the center C—C bond. The ball-and-stick models of the corresponding *n*-butane molecules are shown in Figure 1.21.

The scheme of naming a secondary hydrocarbon group can only be used

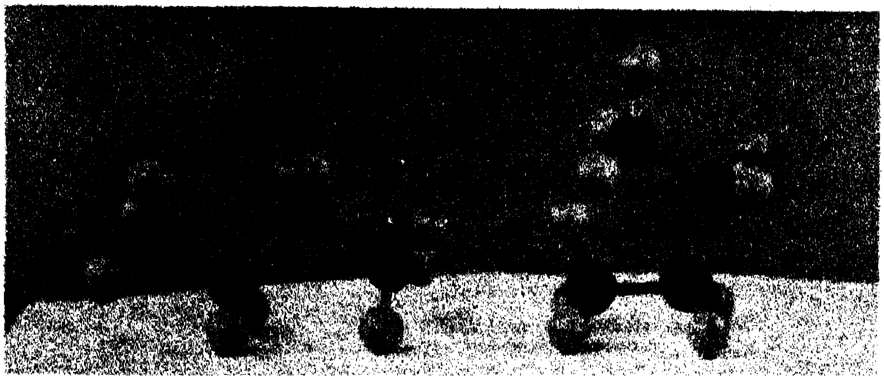


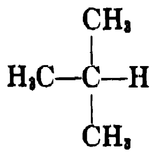
Fig. 1.21. Ball-and-stick models of two conformations of the *n*-butane molecule (either form can be obtained from the other by an 180° rotation of half the molecule about the $C_2—C_3$ bond.)

with butane because the secondary carbons in any other normal hydrocarbon will not be equivalent. For example, from *n*-pentane,

$$CH_3—CH_2—CH_2—CH_2—CH_3,$$

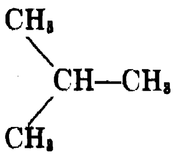
two different secondary groups could result, depending on whether a hydrogen atom is removed from the center carbon atom or from one of those second from an end of the chain. Therefore, the name *sec*-pentyl would be ambiguous. It will be seen presently, when the formal system of nomenclature is taken up, how the two groups are named.

Looking once more at the four butyl groups above, one can see that the four carbon atoms of butane can be arranged such that three are attached to one, giving the structure

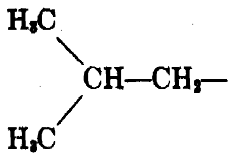


$$\begin{array}{c} CH_3 \\ | \\ H_3C—C—H \\ | \\ CH_3 \end{array}$$

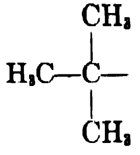
This has the iso- fork in it



and is therefore called *isobutane.* The three methyl groups are equivalent and the three hydrogen atoms on any one methyl group are equivalent; hence, there are nine equivalent hydrogen atoms in the molecule. Removal of one of these nine hydrogen atoms yields the same group, namely, the isobutyl group:



When the hydrogen atom attached to the tertiary carbon in isobutane is removed, there results the *tertiary*-butyl group:



$$H_3C-\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}-$$

As a word of caution, when simple compounds are named on a basis of the type of alkyl group therein, the prefixes iso-, *n*-, *sec*-, *tert*-, etc., are not to be separated from the name of the alkyl group. That is, the name of CH_3—CH_2—CH_2—Br is *n*-butyl bromide, not *n*-bromobutane, and

$$(CH_3)_2CH—Cl$$

is isopropyl chloride, not isochloropropane or chloroisopropyl.

Although a few of the alkyl groups containing more than four carbon atoms have such simple names, the number of cases is quite small. Usually, only the straight-chain groups are so named; that is, *n*-pentyl, *n*-hexyl, and *n*-decyl are the names of groups containing five, six, and ten carbon atoms in a straight chain. Otherwise the groups are named according to the Geneva system as discussed below.

There are over 70 rules in the Geneva system of nomenclature,[10] only a few of which will be needed for compounds encountered at the elementary level. For the aliphatic or open-chain compounds, the general framework of the Geneva system can be summarized by the following four points:

1. The *body* of the name indicates the number of carbon atoms in a continuous chain.
2. The suffix indicates the class of compound, i.e., alcohol, hydrocarbon, acid, ester, etc.
3. The prefix indicates the types and positions of atoms or groups which have been substituted for hydrogen on the main chain, and the location of the functional group.
4. Greek letters are used to refer to carbon atoms in a subchain branched off of the main chain.

This system can best be explained by discussing several examples.

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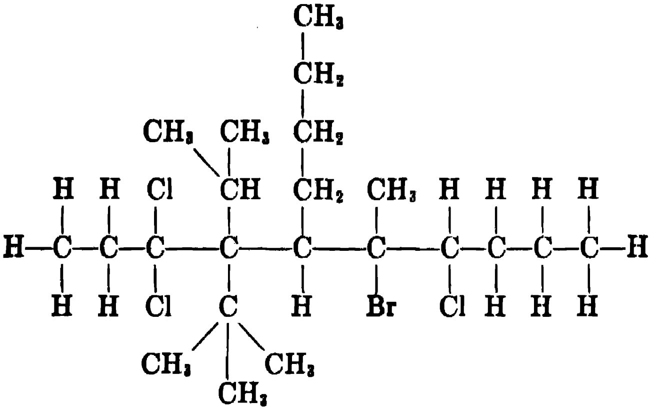
[10] The latest official rules are published in the *Journal of the American Chemical Society* 82, 5545 (1960) and are abstracted in the *Handbook of Chemistry and Physics* and in Lange's *Handbook of Chemistry*. The system of nomenclature used by *Chemical Abstracts* is a modified Geneva system and is described in detail in the Index of the 1945 volume of *Chemical Abstracts*.

As mentioned earlier, the first class of compounds to be studied will be hydrocarbons in which the carbon atoms form only single bonds in open chains. The Geneva name for this family of compounds is *alkane*, and the suffix used to indicate that a substance is a member of this class is *-ane*. In order to have a working vocabulary, the student should learn the names of the first 10 or 12 normal alkanes given in Table 1.7.

TABLE 1.7. NORMAL ALKANES

CH_4	Methane	C_7H_{16}	Heptane
C_2H_6	Ethane	C_8H_{18}	Octane
C_3H_8	Propane	C_9H_{20}	Nonane
C_4H_{10}	Butane	$C_{10}H_{22}$	Decane
C_5H_{12}	Pentane	$C_{11}H_{24}$	Undecane
C_6H_{14}	Hexane	$C_{12}H_{26}$	Dodecane

For illustration, let us work out the name for structure I.



I

The first thing to do is to pick out the longest chain of carbon atoms, that is, the longest extension of carbon atoms through which a needle and thread can be run. It need not be in a straight horizontal line. For instance, in the carbon skeleton of I, there are two ten-atom carbon strings; one string goes straight through horizontally and the other string comes down and turns to our right, as indicated with numbers in Figure 1.22. Thus, one picks out the longest chain with a needle and thread, not with a yardstick.

All other chains have nine or fewer carbon atoms. Either ten-atom carbon chain may be chosen for the main chain. If the L-shaped chain is chosen as the main chain, then that portion of the molecule extending left from carbon atom numbered 5 is to be regarded as a branch chain off the main chain. Similarly, if the straight horizontal chain is selected to be the main chain, then the four carbon atoms extending up from carbon atom 5 is a branch chain. When there are two or more chains to choose for the main chain, that one is usually selected which provides the simplest naming of the branch

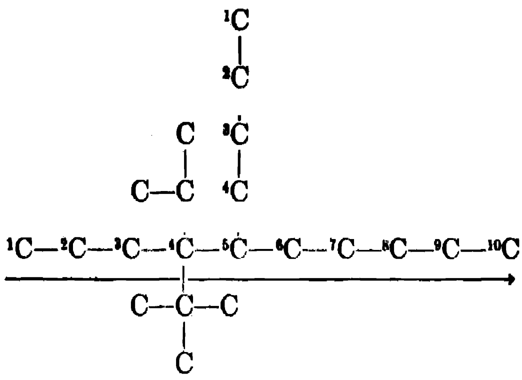
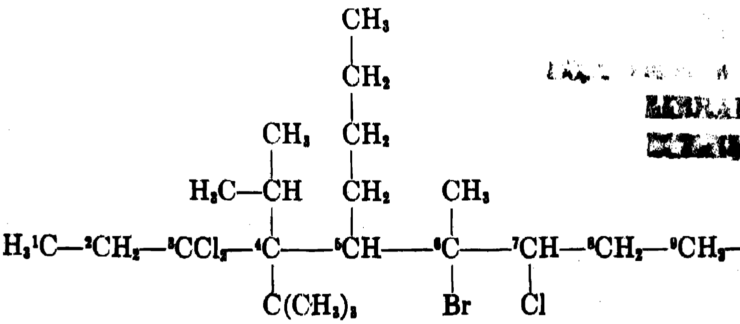


Fig. 1.22. Numbers and arrows to indicate two 10-atom chains in structure I.

chains. In this case, the horizontal chain is chosen, for then the upright branch from C_5 is a simple *n*-butyl group.

After the main chain is selected, the carbon atoms are numbered for reference purposes. One may start at either end of the chain, but it is conventional to start at the end nearest the substituents, for then the prefix numbers which indicate the positions of substituents will be the smaller.

Now, the four initial points of the Geneva system can be followed: (1) The body of the name will be *deca*, based on the fact that there are 10 carbon atoms in the main chain. (2) The suffix is *-ane*, since all the carbon atoms in the main chain form only single bonds. This gives us *decane*, so far. (3) The prefix, indicating the types and positions of substituents, will be more extensive. One goes along the chain from the number 1 carbon atom to the number 10 carbon atom, naming atoms or groups which have been substituted for hydrogen.[11] A carbon atom need not be mentioned unless something has been substituted for hydrogen on that carbon atom. Structure I may be rewritten as Ib, in which the carbon atoms of the main chain have been numbered.



Ib

LIBRARY

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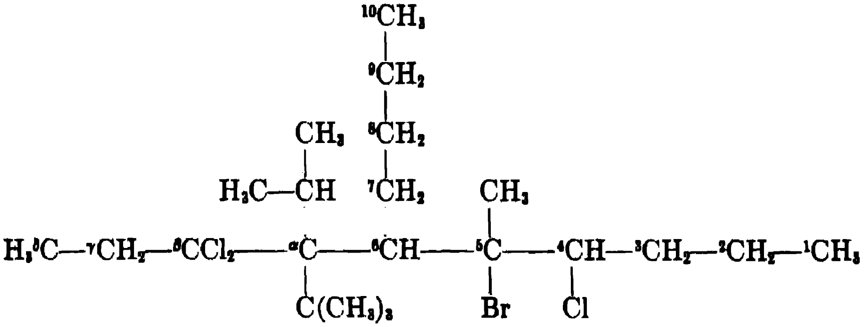
[11] For indexing purposes, the substituents are sometimes listed in alphabetical order irrespective of position.

There are nothing but hydrogen atoms on carbon atoms 1 and 2. On carbon atom 3 there are two chlorines, referred to as 3,3-dichloro-. One could write 3-chloro-3-chloro, but it is simpler and space-saving to combine the two chloros as was first done. Furthermore, if one glances ahead, it can be seen that there is a chlorine atom on carbon atom 7, and rather than name it later, it can be included with the other chlorines and written 3,3,7-trichloro-.[11] On carbon atom 4 there are isopropyl and *t*-butyl groups, giving, so far, 3,3,7-trichloro-4-isopropyl-4-*t*-butyl-. Following this procedure, one can easily see that the complete name of structure I is 3,3,7-trichloro-4-isopropyl-4-*t*-butyl-5-*n*-butyl-6-methyl-6-bromo-decane. This name is unambiguous, and only one structural formula can be written from the name. For practice, draw the graphic formula from the name.

Nevertheless, this is not the only name that can be written for structure I. If the other ten-atom carbon chain had been selected for the main chain, a different name would have been obtained. In other words, a particular compound can have more than one name according to the Geneva system. This is all right as long as the structure conveyed by each of the alternative names is unambiguously the same. For practice, an alternative name for structure I will be worked out, based on the L-shaped ten-atom carbon chain as the main chain.

Notice that point four of the Geneva system was not needed for naming structure I above. It will have to be used this time. The carbon atoms in the main and branch chains are numbered as follows:



$$H_3{}^{\delta}C\text{—}{}^{\gamma}CH_2\text{—}{}^{\beta}CCl_2\text{——}\underset{\substack{|\\C(CH_3)_3}}{\overset{\substack{CH_3\\|\\H_3C—CH\\|}}{{}^{\alpha}C}}\text{——}\overset{\substack{{}^{10}CH_3\\|\\{}^{9}CH_2\\|\\{}^{8}CH_2\\|\\{}^{7}CH_2\\|}}{{}^{6}CH}\text{——}\underset{\substack{|\\Br}}{\overset{\substack{CH_3\\|}}{{}^{5}C}}\text{——}\underset{\substack{|\\Cl}}{{}^{4}CH}\text{—}{}^{3}CH_2\text{—}{}^{2}CH_2\text{—}{}^{1}CH_3$$

Ic

The numbering begins at the right-hand end this time because that places the first substituent on carbon atom 4, whereas if the numbering started at the top carbon atom (the present carbon atom 10), then the first substituent would be on the fifth carbon atom in the chain. So, the name starts off with 4-chloro-5-methyl-5-bromo-6-. On carbon atom 6 there is a complex subtuent. It is a branched chain within which the longest string of carbon atoms is four atoms long. A four-atom carbon chain is a butyl group, but this butyl group contains substituents. In order to indicate what type and where the substituents are attached, the carbon atoms in the butyl group are numbered or lettered. Usually there will be no doubt, but to avoid confusion with the numbering on the main chain, the carbon atoms in the branch are designated differently. The I.U.C. rule equally permits Greek letters, ordinary letters, primed numbers (1′, 2′), numbers with indices (6^1, 6^2), or other notations. Greek letters are most commonly used, and they will be adopted here. The lettering always starts at the carbon atom by which the group is attached to the main chain.

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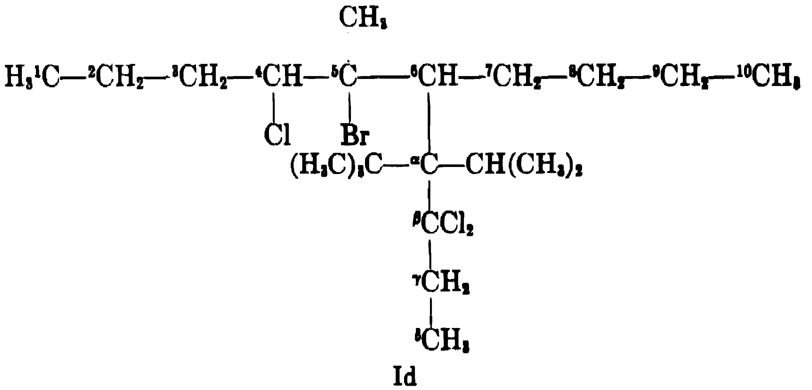
[11] Some students think that 3,3,7-trichloro- would mean two *trichloro* groups on C_3 and one on C_7, even if there were a trichloro group. There is no such group. It is to be realized that there will be a substituent for each number and a number for each substituent. If three numbers are given, then there must be three substituents.

Continuing to name compound I, then, as numbered in Ic, at carbon atom 6 there is the substituted butyl group. To show clearly that the description of the branch refers just to the branch, parentheses are used. Thus, one has here, 6-(α-isopropyl-α-*t*-butyl-β,β-dichlorobutyl)-. The complete name is 4-chloro-5-methyl-5-bromo-6-(α-isopropyl-α-*t*-butyl-β,β-dichlorobutyl)-decane. For practice, write out the graphic formula of this compound from the name. Notice that when this is done, a structure such as Id will be obtained, where the complex branch on C_6 extends up or down.

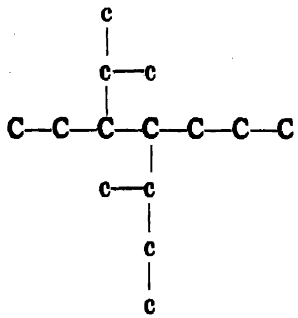


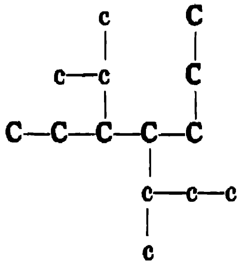
Id

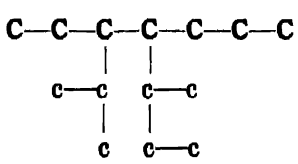
Structure Id develops from the name above because, from the portion decane, one first writes down ten carbon atoms in a horizontal row, then attaches the substituents to this chain of atoms as they are cited in the name. At first glance I and Id do not appear to be the same molecule, and Ic and Id appear to have switched ends. This is so and is to be expected, because molecules can have any orientation in space. Another way to think of it is that in Id the molecule is numbered from left to right, but to a person behind the page it appears to be numbered from right to left, or as it appears to the reader in Ic. Whether one numbers from right to left or from left to right depends upon whether one is looking at a molecule from one direction or from the opposite direction.

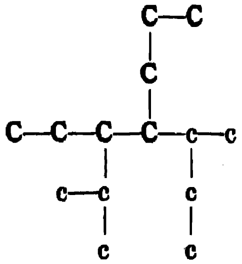
Also, the butyl group which comprises carbon atoms 7 to 10 in Id extends out straight, but in Ic it was bent upward. Notice that if the $^5C—^6C$ carbon-carbon bond in Id were to rotate 120°, it would swing the $^7C—^{10}C$ carbon chain upward and bring the $^{\alpha}C—^{\gamma}C$ branch level with the $^1C—^6C$ chain, as the molecule appears in Ic. Because of the ease of rotation, this may happen so that two samples of the material cannot be obtained in which all the molecules in one sample would have configuration Ic and all molecules in the other sample would have configuration Id. The ease at which one configuration passes into the other prevents the isolation of a sample in which all molecules have only one configuration. Actually, molecules do not assume all possible configurations but only those that are the most stable.

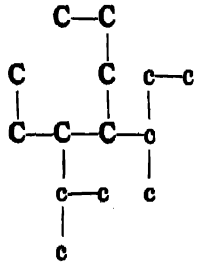
Because of such rotation, one must get accustomed to seeing the same group twisted in one of several possible configurations. For example, the following configurations may be given for 3-isopropyl-4-*sec*-butylheptane, and they differ merely by rotations about various C—C bonds. To avoid confusion, only the carbon skeletons are shown, and the same seven-atom chain is in bold face in each structure for the student's orientation.











Many others could be given. The point to be emphasized is that organic molecules, in the liquid or gaseous states or in solution, are twisting about like this continuously. This is particularly true for long-chain molecules.

One additional point about nomenclature can be mentioned. In a strict sense, any organic compound can be considered as a derivative of methane where various groups have been substituted for one or more of the methane hydrogens. Thus, $(CH_3)_2CH—CH_2—CH_3$ may be called dimethylethylmethane, or isopropylmethylmethane, or isobutylmethane, where first the third from right, then the second from right, then the right-end carbon atom is regarded as the methane carbon atom. This scheme can be used for simple molecules without any difficulty, although sometimes it is illogical. It is often absurd for complex molecules.

When a compound is named as a derivative of an actual substance, the name is written as one word, with hyphens used to separate numbers or just for clarity. Thus, propane is a definite compound, and names of its derivatives are written as one word, as for example, 1-chloropropane or 2-hydroxypropane. On the other hand, chloride and alcohol are not the names of actual compounds but of two classes of compounds. Hence, *n*-propyl chloride or isopropyl alcohol (for the two compounds just mentioned) are each written as two words.

This section has covered the basic points of the Geneva system. There are several additional rules to be learned which take care of the various classes of open-chain and cyclic structures. These rules will be incorporated into the system as new classes of compounds are encountered.

It is noteworthy that the Geneva system is continually being revised in order to take care of new, complex organic molecules. In recent years chemists have been trying to develop systems for the codification of organic substances. Particularly for card indexing, a system of linear notation is sought which would provide a unique code name or line formula for each compound and which would reveal as much information as possible about the compound. Several systems have been devised, and for examples, the code names of two compounds by four of these systems are as follows:

Common Name	*Dyson*	*Gruber*	*Silk*	*Wiswesser*
Isopropyl alcohol	C_3.Q,2	C3.20H	CQC	QY
Benzoic acid	B6.CX	(6)CX	B.X	QVR

These systems are receiving critical evaluation by international committees with respect to speed of coding and decoding names, simplicity, ability to handle all types of structures, and other pertinent points.

1.6 ISOMERISM

As defined in Section 1.1, isomers (Gr., *isos*, the same, and *meros*, parts) are substances having the same molecular formula but different molecular structures. Isomerization is the process of going from one isomer to another, and isomerism is the phenomenon that isomers exist. Several forms of isomerism are possible and these are outlined in Table 1.8.[13]

TABLE 1.8. OUTLINE OF TYPES OF ISOMERS

A. Structural Isomers	*B. Stereoisomers*
1. Chain	1. Geometric
2. Position	2. Optical
3. Functional	

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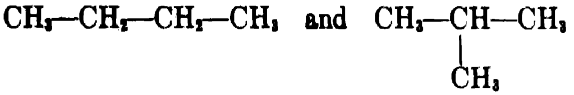
[13] It will be seen later that certain types of isomers which still fall under this general classification are denoted by special names such as tautomers, epimers, anomers, and conformers.

The difference between structural and stereoisomers can be described as follows. Two or more structural isomers contain the same types and number of atoms but the combinations of bonded pairs of atoms will be different in each isomer. In two or more stereoisomers, there will be the same combinations of bonded pairs of atoms but their orientation in space will be different. That is, the same respective atoms are bonded to one another in stereoisomers but their relative, spatial positions are different. These descriptions will become clearer when examples are considered.

1. *Chain isomers.* Such isomers differ in the shape of the carbon skeleton; examples are



$$CH_3—CH_2—CH_2—CH_3 \quad \text{and} \quad CH_3—\underset{\displaystyle CH_3}{\underset{|}{CH}}—CH_3$$

n-Butane Isobutane

2. *Position isomers.* Such isomers differ in the positions of some reference atom or group; examples are

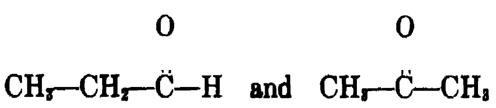
$CH_3—CH_2—CH_2—CH_2—CH_2Cl$	1-Chloropentane
$CH_3—CH_2—CH_2—CHCl—CH_3$	2-Chloropentane
$CH_3—CH_2—CHCl—CH_2—CH_3$	3-Chloropentane

Observe that 4-chloropentane is the same molecule as 2-chloropentane, and 5-chloropentane is identical to 1-chloropentane.

3. *Functional isomers.* Such isomers differ by having different functional groups present; examples are

$$CH_3—O—CH_3 \quad \text{and} \quad CH_3—CH_2—O—H$$

Methyl ether Ethyl alcohol

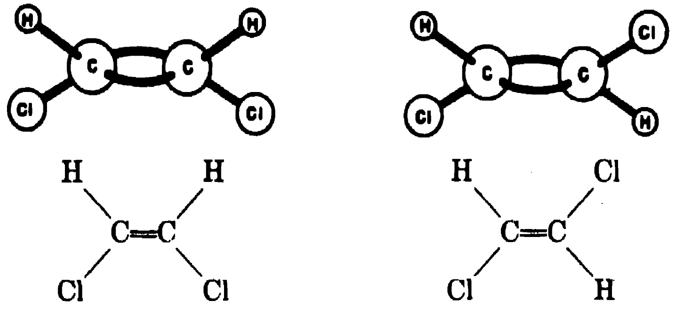


$$CH_3—CH_2—\overset{\displaystyle O}{\overset{\|}{C}}—H \quad \text{and} \quad CH_3—\overset{\displaystyle O}{\overset{\|}{C}}—CH_3$$

Propionaldehyde (an aldehyde) Acetone (a ketone)

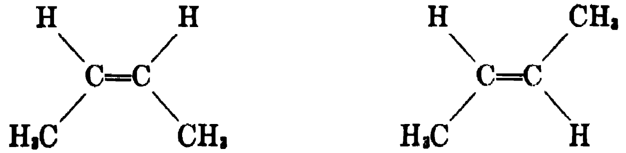
Notice that the last two isomers are also position isomers because they differ in the positions of the C=O group. Thus two or more compounds may exhibit more than one form of isomerism. Notice too that for all the examples given, the same specific atoms are not joined to one another in any particular set of isomers. For example, in (2) a chlorine atom is attached to either the first, second, or third carbon atom in the pentane chain, and in the case of isomeric methyl ether and ethyl alcohol, an oxygen atom is between two carbon atoms in the ether, and between a carbon atom and a hydrogen atom in the alcohol.

4. *Geometric isomers.* These are isomers which differ in their spatial structures about some plane through the molecule. The most frequent case among organic molecules is for two atoms or groups to be either on the same side or on opposite sides of a double bond within the two molecules. The former is called the *cis isomer* and the latter the *trans isomer*. Therefore, such isomerism is commonly referred to as *cis-trans isomerism*. For example, models and structural formulas for the *cis* and *trans* isomers of 1,2-dichloroethylene and of 2-butene are shown in Figure 1.23.



cis-1,2-Dichloroethylene

trans-1,2-Dichloroethylene



cis-2-Butene
B.p. = 3.73°

trans-2-Butene
B.p. = 0.3°

Fig. 1.23.

Isomerization from the *cis* to the *trans*, or vice versa, is restricted because of the double bond. Rotation about the C═C bond is prevented, just as is rotation of two blocks when two nails are driven through them (Figure 1.24). Therefore, once either geometric isomer has been formed, it remains as such. Because of slightly different physical properties such as boiling points, solubilities, etc., a mixture of the two isomers can usually be resolved and the individual isomers collected in separate containers. In contrast to this, the *gauche* and *trans* forms of ethylene chloride (1,2-dichloroethane)

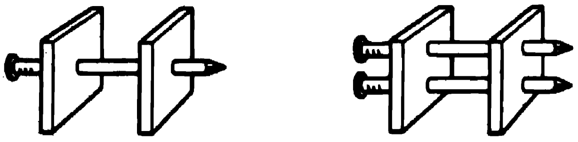
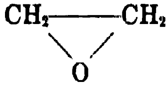


Fig. 1.24. Rotation about single nail is easy (*left*). Rotation is prevented by presence of two nails (*right*).

cannot be collected in separate vessels because of the "spontaneous" transformation of either form into the other by easy rotation about the C—C single bond.

Some 1,2-disubstituted ethanes have trivial names based on a system of nomenclature used before the adoption of the Geneva system. Thus, 1,2-dichloroethane is called *ethylene chloride*. The name may be confusing because the compound does not possess a C=C bond as suggested by the name ending, *-ene*. On the other hand, 1,2-dichloroethylene, $HClC{=}CHCl$, does have a C=C bond. The names of the two types of compounds differ in the fact that substituted ethylenes (C=C compounds) have the names of the substituents preceding and attached to the word *ethylene* while 1,2-disubstituted ethanes have names of substituents to follow the word *ethylene*. Several other common 1,2-disubstituted ethanes are

Ethylene bromide	$Br{-}CH_2CH_2{-}Br$
Ethylene g'ycol	$HO{-}CH_2CH_2{-}OH$
Ethylene chlorohydrin	$Cl{-}CH_2CH_2{-}OH$
Ethylene cyanohydrin	$HO{-}CH_2CH_2{-}CN$
Ethylene oxide	

The second form of stereoisomerism arises when there is no plane of symmetry in a molecule. For example, the tetrahedral model of fluorochlorobromomethane would look like Figure 1.25 (some attention being given to relative sizes of atoms). Observe that an imaginary plane, about which one side would be a mirror image of the other side, cannot be passed through the molecule, whereas this is possible for fluorochloromethane (Figure 1.26).

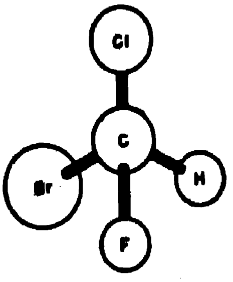


Fig. 1.25.

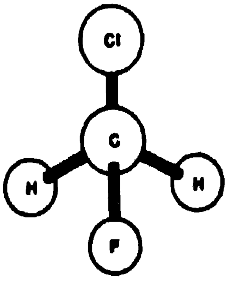


Fig. 1.26. Plane of symmetry passes through the Cl—C—F axis.

The most common organic molecules lacking a plane of symmetry are those in which at least 1 carbon atom has 4 different atoms or groups attached to it. Whenever this is the case, there will be two alternative arrangements of the groups about the carbon atom, such that the two resulting molecules are mirror images of each other. That is, when either molecule is placed before a mirror, its reflection is identical to the other isomer (Figure 1.27).

Neither molecule is identical to the other; that is, the two molecules will not fit into the same mold, just as a person's two hands cannot wear the same glove. Their resemblance is that of mirror images. Most of the properties are the same for two such isomeric molecules except their effect upon a beam of polarized light, and for this reason they are referred to as *optical isomers*. One isomer rotates a beam of polarized light to the left and the other isomer rotates the beam an equal angle to the right, and the two isomers are referred to as the *levo* and the *dextro isomer*, respectively. Much more will be said about optical isomerism in Chapter 17, and what has been said here will suffice for the discussions until that time.

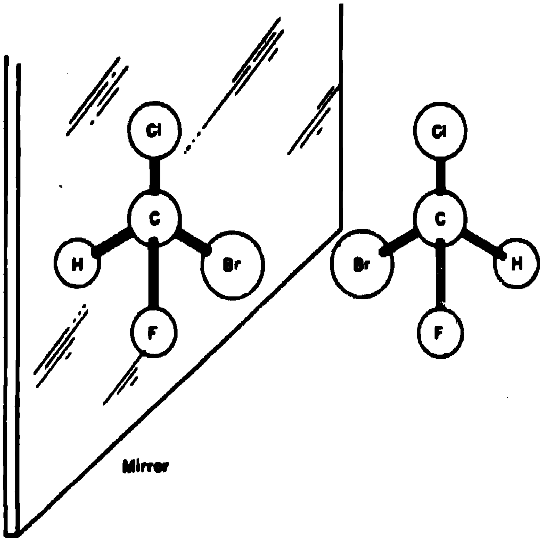


Fig. 1.27.

Notice that for the two types of stereoisomerism the same specific atoms are joined to one another in a pair of isomers, but the two structures differ in their spatial configuration. This is the difference between stereoisomerism and structural isomerism.

The phenomenon of isomerism is responsible for the great difference in the number of known organic and inorganic compounds. For instance, from just the aliphatic hydrocarbons, the numbers of possible isomers are given in Table 1.9. Obviously only a very small fraction of these compounds has been isolated. All of the predicted alkanes through the nonanes and most of the decanes are known. Considering the fact that by including other elements, the number of theoretically possible isomers with a given molecular formula will be many times the numbers given just for hydrocarbons, then the total potential number of different organic substances is beyond comprehension.

TABLE 1.9. CALCULATED NUMBERS OF ISOMERS FOR SATURATED ALIPHATIC HYDROCARBONS

Formula	Cal'd Number of Isomers	Formula	Cal'd Number of Isomers
CH_4	1	$C_{11}H_{24}$	159
C_2H_6	1	$C_{12}H_{26}$	355
C_3H_8	1	$C_{13}H_{28}$	802
C_4H_{10}	2	$C_{14}H_{30}$	1,858
C_5H_{12}	3	$C_{15}H_{32}$	4,347
C_6H_{14}	5	$C_{16}H_{34}$	10,359
C_7H_{16}	9	$C_{20}H_{42}$	366,319
C_8H_{18}	18	$C_{30}H_{62}$	4,111,846,763
C_9H_{20}	35	$C_{40}H_{82}$	62,491,178,805,831
$C_{10}H_{22}$	75	$C_{60}H_{122}$	2.2×10^{22}

In the discussions on nomenclature and stereoisomerism, mention was made of the ease of rotation about single bonds. In the earlier literature this was often called *free rotation*, and the term arose because isomers could not be isolated or even detected in compounds such as 1,2-dichloroethane. Thus, rotation of the CH_2Cl groups about the C—C bond in 1,2-dichloroethane can give rise to many relative orientations of the two groups, but three are of particular interest. These are the *trans*, the *gauche*, and the *cis* conformations shown in Figure 1.28. The term *conformation* refers to the various configurations of a molecule which differ in space by a rotation of two atoms about a

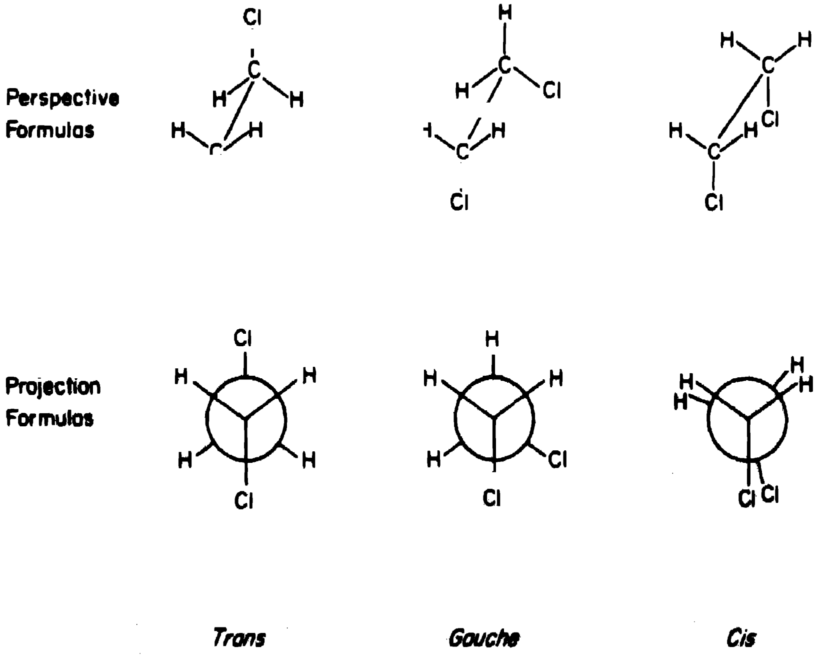


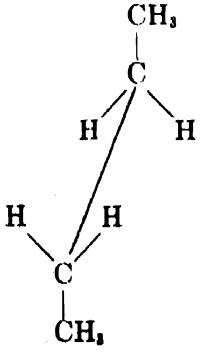
Fig. 1.28. Conformations of the 1,2-dichloroethane molecule.

single bond. Certain conformations of a molecule are energetically favored and have a finite existence. This is really a special type of stereoisomerism, and isomers having different conformations are called *conformers*. The study of the physical and chemical properties of a compound in relation to its geometry and population of its conformers is called *conformational analysis*.

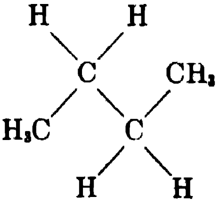
The atoms in the *trans* and *gauche* conformations of 1,2-dichloroethane are said to be *staggered*, and they are *eclipsed* in the *cis* conformation. That is, as you look along the C—C axis of the *cis* molecule, the atoms attached to the front carbon block out those on the rear carbon atom. There is a repulsion between nonbonded atoms which increases as the atoms approach one another. Consequently, this repulsion is greatest in the *cis* conformation and least in the *trans*, to make the *trans* conformer the most stable and the *cis* conformer the least stable. The *gauche* conformation has a staggered arrangement too, but here the large chlorine atoms are closer together than any two atoms in the *trans* conformation, which makes the *gauche* conformer about 1.4 kcal/mole less stable than the *trans*.

Now, 1,2-dichloroethane, as well as most conformational mixtures, exists as an equilibrium mixture of the *trans*, *gauche*, and *cis* conformations at any given temperature with the *cis* being present in very small amounts except at high temperatures. The energy required to change one conformation into the other is called the energy barrier to internal rotation. It is about 2.8 kcal/mole in the case of the *trans* to *gauche* transformation of 1,2-dichloroethane. Most often these energy barriers to rotations about single bonds are not large enough to prevent one conformation from changing "spontaneously" into another in the liquid or vapor state. Consequently, it is unusual to be able to isolate pure samples of a single conformation of a compound. Later, however, we will discuss certain cases where the barrier to rotation is sufficiently large to permit the isolation of different conformers of a molecule (cf. Section 8.3).

Similarly in *n*-butane, the carbon chain preferably assumes the *gauche* conformation in which methyl groups occur in place of chlorine atoms of 1,2-dichloroethane.

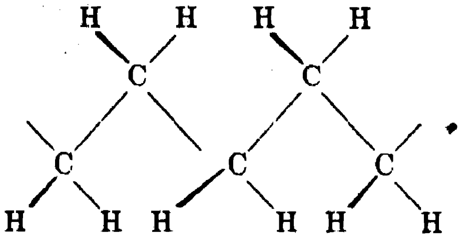


End-on view of *n*-butane



Side view of *n*-butane

The side view of *n*-butane reveals the Z-shaped configuration of the carbon chain in the *trans* conformer, and it can be understood why a saturated hydrocarbon carbon chain has a zig-zag shape.



In this conformation, each CH_2 group is *trans* across the C—C bond to give the least amount of repulsion between neighboring groups.

STUDY EXERCISES

1. Write the structural formulas for (a) the first ten normal alkanes; and (b) the methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, *tert*-butyl, *sec*-butyl, and the *n*-decyl groups.

2. Write graphic formulas for the following compounds:

(a) 2-methyl-3-ethylhexane
(b) 3,3,4-trimethylheptane
(c) 4-isopropyl-6-methylnonane
(d) 3-*tert*-butyl-4-*sec*-butyl-5-*n*-butyl-6-chloromethyldecane.

3. Name the following compounds:

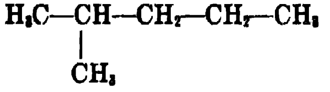
(a) $(CH_3)_2CH-CH(C_2H_5)-CH_2-CH_2-CH_2-CH_3$
(b) $CH_3-CH_2-C(CH_3)_2-CH(CH_3)-CH_2-CH_2-CH_3$
(c) $CH_3-CH_2-CH_2-CH(CH_2Cl)-CH_2-CH_3$

4. Give an example of chain, position, functional, geometric, and optical isomers.

5. Pick out the primary, secondary and tertiary carbons in the molecules of Problem 2.

TEST QUESTIONS, Set 1

1. Give three names for the compound



$$H_3C-\underset{\displaystyle CH_3}{\underset{|}{CH}}-CH_2-CH_2-CH_3$$

2. Give the graphic formulas and names for the isomers having the molecular formula $C_5H_{11}Br$ (8 possible).

3. Give the structural formulas and names for the isomers having the molecular formula $C_5H_{10}Br_2$ (21 possible).

4. What are the structural formulas for neopentane and the neopentyl group?

5. Which formulas in the following list represent identical molecules:

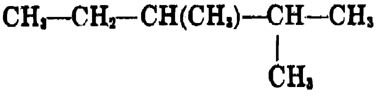
(a) $CH_3{-}CH(CH_3){-}CH_2{-}CH_3$

(b) $CH_3{-}CH(C_2H_5){-}CH(CH_3)_2$

(c) $CH_3{-}CH_2{-}CH(CH_3)_2$

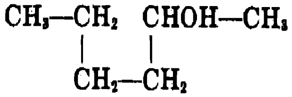
(d) $CH_3CH_2CHOHCH_2CH_2CH_3$

(e)



$CH_3{-}CH_2{-}CH(CH_3){-}\underset{\displaystyle CH_3}{\underset{|}{CH}}{-}CH_3$

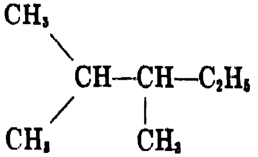
(f)



$$\begin{array}{l}CH_3{-}CH_2\quad CHOH{-}CH_3\\ \qquad\quad |\qquad\quad\;\; |\\ \qquad\;\; CH_2{-}CH_2\end{array}$$

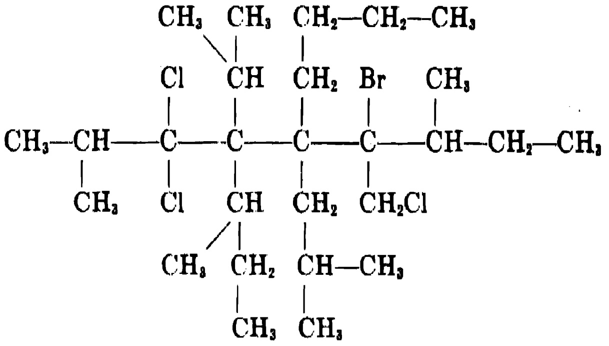
(g) $(CH_3)_2{-}CH{-}C_2H_5$

(h)



6. Write line formulas for the following compounds: (a) 2,2,3-trimethylhexane; (b) 3-methyl-4-*n*-propyloctane; (c) isohexane; (d) neohexane.

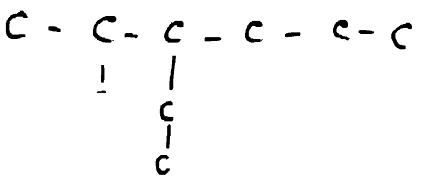
7. Give a name for the following compound:



8. Give the structural formula for 1,1-dibromo-4-isopropyl-4-*n*-propyl-5-*tert*-butyl-5-(α-chloro-γ-methylbutyl)-7-chloromethylnonane.

9. Write electronic structures for water, ammonia, methane, nitric acid, nitrous acid, sulfuric acid, and ammonia-boron trifluoride.

10. If a compound B is ten times as soluble in ether as it is in water, will the distribution coefficient be larger when using brine instead of water? Why, or why not?



2

Alkanes

2.1 ALIPHATIC ORGANIC CHEMICALS

One striking fact about aliphatic chemicals is the big change in their sources over the past 35 years. In 1927 less than 0.1 per cent of the aliphatics came from natural gas and petroleum and over 80 per cent came from plants. Today plants supply about one-fourth of all aliphatic chemicals, and one-half come from petroleum and natural gas (Figure 2.1).

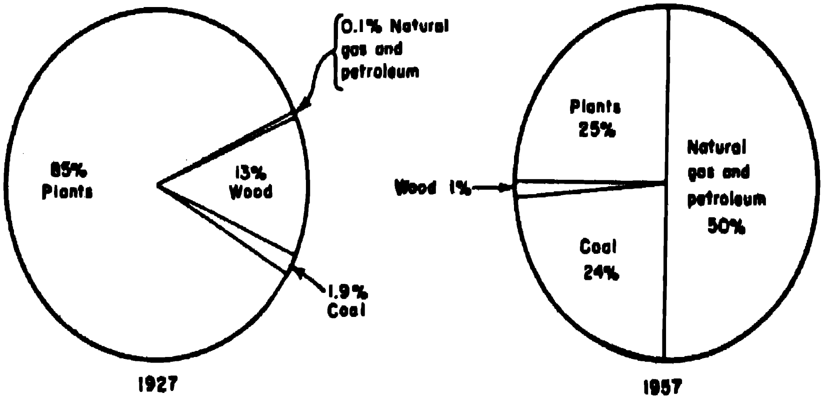
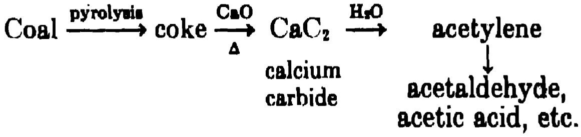


Fig. 2.1. Sources of aliphatic chemicals.

Aliphatics are produced from plants chiefly by fermentation, with a few being isolated by extraction. By the pyrolysis of wood (Gr. *pyr*, fire, and *lysis*, loosing) there can be obtained methyl alcohol, acetic acid, and acetone. Sometimes the process is called *destructive distillation*, and is merely the thermal decomposition of a material by heating it to an elevated temperature in the absence of air. As Figure 2.1 shows, this source of organic chemicals is now used very little; compounds are being produced today from natural gas, petroleum, and coal. Natural gas and petroleum are mixtures of hydrocarbons with small amounts of sulfur and nitrogen-containing compounds mixed therein. Consequently, natural gas and petroleum merely need to be resolved to yield various hydrocarbons which subsequently may be converted into their many useful derivatives. Coal is a carbonaceous material in which the carbon atoms form various types of rings, and when it is pyrolyzed it yields primarily aromatic chemicals, leaving coke as a residue. It is, therefore, the chief source of aromatic chemicals. However, as a result of seeking a supplement to the supply of gasoline during World War II (which comes chiefly from petroleum), methods were found in which gasoline and fuel oil could be produced from coal. Low molecular weight, oxygenated aliphatic chemicals, such as methyl alcohol, acetic acid, and acetone, are produced as side products. The other general route from coal to certain aliphatics is through the series of steps



$$\begin{tikzcd}
\text{Coal} \arrow[r, "\text{pyrolysis}"] & \text{coke} \arrow[r, "\text{CaO}", "\Delta"'] & \underset{\substack{\text{calcium}\\ \text{carbide}}}{CaC_2} \arrow[r, "H_2O"] & \text{acetylene} \arrow[d] \\
& & & \substack{\text{acetaldehyde,}\\ \text{acetic acid, etc.}}
\end{tikzcd}$$

This was Germany's lifeline for her chemical industry during World War II because she had no natural source of petroleum but did have an abundant supply of coal.

The distribution of uses of aliphatic chemicals is shown in Table 2.1.

TABLE 2.1. APPROXIMATE DISTRIBUTION OF USES OF ALIPHATIC CHEMICALS

	Per cent	*Uses*
Synthetic rubber	25	Tires and tubes, etc.
Automotive	20	Antifreeze, lead tetraethyl, etc.
Plastics and resins	17	Almost every conceivable use
Textiles	14	Rayon, nylon, etc.
Surface coatings	8.4	Alkyd paints, etc.
Metal processing	5	Solvents for degreasing, etc.
Explosives	4	Dynamite, RDX, etc.
Foods	3	Fertilizer, refrigerants, etc.
Medicinals	1.1	Anesthetics, etc.
Miscellaneous	2.5	

2.2 NOMENCLATURE OF ALKANES

The alkanes are generally the first family of organic compounds to be studied because the other classes of compounds may be regarded as substitution products of the alkanes and the alkanes are easily obtained from natural resources. They are characterized by the fact that they consist of carbon and hydrogen only, and that the carbon atoms form only single bonds in open-chain structures. When other atoms or groups have been substituted for any of the hydrogens in an alkane, the product is regarded as a derivative of the original alkane. The ratios of hydrogen to carbon atoms in all of the alkanes fit the *general empirical formula* C_nH_{2n+2}, in which n is the number of carbon atoms per molecule. For example, CH_4, C_2H_6, C_3H_8, C_5H_{12}, and $C_{10}H_{22}$ are molecular formulas for certain alkanes. If the molecular formula of a hydrocarbon is not consistent with C_nH_{2n+2}, then it is not an alkane. For instance, C_6H_{12}, C_8H_{16}, and C_3H_6 are not alkanes. All the normal alkanes up to $C_{70}H_{142}$ and a few scattered members beyond this one have been prepared.

In order for carbon to maintain its quadrivalence in open-chain compounds in which the ratios of hydrogen to carbon are less than $2n + 2$, the carbon atoms must form one or more multiple covalent bonds, i.e., double or triple bonds. Compounds containing multiple bonds tend to add other compounds to the multiple bonds. It is as if the combining power or total valency of the atoms forming multiple bonds *is not entirely used up and they try to do so* by forming bonds with additional atoms. Because of this, compounds containing multiple bonds are referred to as being *unsaturated*, and compounds containing only single covalent bonds are called *saturated* compounds.

Therefore, alkanes may be defined as saturated, aliphatic hydrocarbons. Compared to other classes of compounds, the alkanes are quite inert to common chemical reagents and for this reason, they are called *paraffin* (L., *parum*, small, and *affinis*, akin) *hydrocarbons.*

In general, for each of the classes or families of organic compounds which will be taken up, their nomenclature, industrial and laboratory preparation, physical and chemical properties, and occasionally their uses will be discussed. The nomenclature of the alkanes was discussed in Section 1.5, although the names of a few of the alkanes beyond dodecane can be added. Based on the number of carbon atoms they contain, the names are as follows:

C_{13}	Tridecanes	C_{23}	Tricosanes
C_{14}	Tetradecanes	C_{30}	Triacontanes
C_{15}	Pentadecanes	C_{35}	Pentatriacontanes
C_{20}	Eicosanes	C_{40}	Tetracontanes

2.3 PREPARATION OF ALKANES

V V. 1. **Laboratory preparation.** Usually several laboratory methods of preparing each class of organic compound will be taken up. Frequently the conditions or required starting material for one method are unavailable, but are obtainable for a second method. Sometimes there will be a large number of methods of preparing a particular family of compounds, but only the most common or those of greatest usefulness will be given.

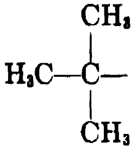
As stated in the Preface, many of the organic reactions studied in elementary organic chemistry have to be committed to memory. Rote memorization will not be sought, however. The reactions will be employed for various types of operations, such as synthesis, analysis, separations, etc., and through this variety of associations, the reactions will soon be learned. For this reason the student should use as many senses as possible in his studying. He is strongly urged to study in small groups rather than alone, so that he may write, hear spoken, and speak chemical terms and formulas. Writing is especially effective for remembering material. The student who easily understands the lectures or the textbook should be warned particularly, because he will be less inclined to study by writing and will find that when he is required to write organic equations or describe the chemical properties of given compounds without the use of his notes or book, he is unable to recall the material accurately. Furthermore, group study gives the student some confidence and experience in expressing what he has learned; and finally, it allows each student to pick up points he may have missed in lecture and to get different viewpoints on the same lecture material.

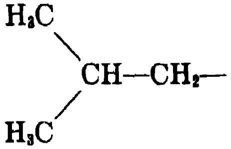
(*i*) *Reduction of alkyl halides*

$$R{-}X \xrightarrow{\text{R.A.}} R{-}H$$

R.A. = reducing agent
Zn, HCl
$LiAlH_4$
HI + P
H_2 + cat.
Mg, then H_2O

This is what is called a *general equation* for a type-reaction. That is, the equation expresses a type of reaction which is common for a given class of compounds and may be used for any member of the family of compounds. The letter X is conventionally used in organic chemistry to represent a halogen atom (normally excepting fluorine). Organic halides have similar properties but differ in reactivity in the order I > Br > Cl ≫ F. This reduced reactivity of the fluorine compounds has led to their being studied separately from the other halogen compounds. Heavy use is made of the symbol R. In the present case it represents any alkyl group, and R—X and R—H would be the corresponding alkyl halide and alkane, respectively. Thus, if one wants to prepare ethane by this reaction, R would be an ethyl group; if isobutane is wanted, the R may be either a *t*-butyl group or an isobutyl group,





for when a hydrogen atom is added to either group at the open bond, isobutane results.

As indicated above, a number of reducing agents may be used to convert an alkyl halide to an alkane, and five common ones will be presented here.

1. Zinc in concentrated hydrochloric acid is a strong reducing agent and can be used for this reduction.

$$RCl + Zn + HCl \rightarrow RH + ZnCl_2$$

2. Lithium aluminum hydride, $LiAlH_4$, is a postwar reagent and finds extensive use in organic chemistry. It is quickly oxidized by water vapor in the air, so it is used in a dry organic solvent. After the $LiAlH_4$ is allowed to react with the alkyl halide, the intermediate complex is hydrolyzed in dilute acid to yield the alkane.

$$4RX + LiAlH_4 \rightarrow 4RH + LiX + AlX_3$$

Primary alkyl halides react more easily than secondary, and tertiary with difficulty. This reaction is useful for the introduction of deuterium atoms into a molecule by using $LiAlD_4$ in place of the $LiAlH_4$ to give R—D.

3. Hydrogen iodide is a powerful reducing agent, but the iodine which is produced will react with the alkane in this case. All the halogens react with phosphorus very rapidly; hence, phosphorus is added to this reaction mixture to remove the iodine as it is formed.

$$\begin{array}{c} 3RX + 6HI \rightarrow 3RH + 3I_2 + 3HX \\ 3I_2 + 2P \rightarrow 2PI_3 \\ \hline 3RX + 6HI + 2P \rightarrow 3RH + 3HX + 2PI_3 \end{array}$$

4. Catalytic hydrogenation is a clean-cut reaction, but not commonly carried out in the student laboratory because it requires more elaborate apparatus than is usually found in large elementary classes. Hydrogen always requires a catalyst for reaction, which for chemical reductions is usually platinum, palladium, or nickel. The metals are especially treated to give their surfaces catalytically active centers.

$$RX + H_2 \xrightarrow{\text{cat.}} R\text{—}H + HX$$

5. Magnesium reacts with alkyl halides to give a substance, RMgX, known as a *Grignard reagent*. Grignard reagents will be used in connection with almost every class of organic compound. They have two very characteristic chemical properties, one of which is to react with any substance having an active hydrogen atom (an active hydrogen atom is one that is readily replaced by a metallic cation, such as is found in water and protonic acids). In such a reaction, the R group of the Grignard reagent takes the active hydrogen to form R—H, and the MgX takes what is left. Hence, with water, one gets an alkane:

$$RMgX + HOH \rightarrow R\text{—}H + MgXOH$$

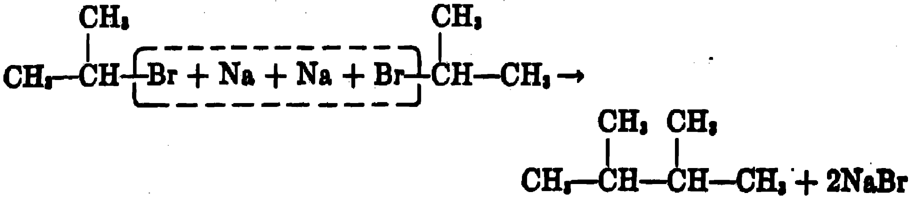
Since the reaction is carried out in two stages but in one reaction vessel, the water is indicated by "then H_2O." Therefore, the over-all reduction is indicated as

$$R\text{—}X + Mg \xrightarrow{\text{then } H_2O} R\text{—}H + MgXOH$$

(*ii*) *The Wurtz reaction:*

$$2R\text{—}X + 2Na \rightarrow R\text{—}R + 2NaX.$$

For illustration, 2,3-dimethylbutane may be prepared from isopropyl bromide.



$$CH_3-\underset{}{\overset{CH_3}{\overset{|}{C}H}}-Br + Na + Na + Br-\overset{CH_3}{\overset{|}{C}H}-CH_3 \rightarrow CH_3-\overset{CH_3}{\overset{|}{C}H}-\overset{CH_3}{\overset{|}{C}H}-CH_3 + 2NaBr$$

If two different alkyl halides are used together, R—X and R′X, then coupling will occur to give R—R′, R′—R′, and R—R. Thus a mixture of three different products is formed whose resolution is usually a difficult task in the laboratory. Ignoring differences in reactivity, the statistical proportion of the three products is 50% R—R′, 25% R—R, and 25% R′—R′. Consequently, only symmetrical alkanes are prepared by this reaction for which a single alkyl halide is used. Possible mechanisms for this reaction were given in Section 1.2.

(*iii*) *Electrolysis of carboxylic acid anions*

$$R-COO^- \xrightarrow[\text{Anode}]{-e^-} R-COO\cdot \xrightarrow{-CO_2} R\cdot \xrightarrow{\text{dimerization}} R-R$$

This reaction is known as the *Kolbe electrolysis*. The carboxylate anion gives up an electron to the anode (oxidation) to become a free radical. One theory is that this first free radical loses carbon dioxide to form an alkyl free radical that quickly dimerizes to the hydrocarbon.

b. Industrial production of alkanes. Frequently laboratory and commercial methods of preparing organic chemicals differ; they are therefore taken up separately. The methods differ for three major reasons:

1. The primary interest of industry is to make money. Therefore in the production of an organic chemical, industry uses the method which has the lowest over-all cost, taking into account the necessary starting materials and equipment, shipping costs, and the potential sales of any side products.
2. The commercial value of side products is an important item. For example, say that a company has an order for methyl bromide and it makes the methyl bromide by the bromination of methane. It was shown in Section 1.2 that bromination of methane yields methyl bromide, dibromomethane, tribromomethane, and tetrabromomethane. Although the company would prefer to convert all of the methane into methyl bromide, there is no significant loss from a portion of the methane being converted into the other bromination products, because the company merely places these side products in stock. Later, when an order comes in for any of the side products, it has them ready for sale, and the income from the sale of side products reduces the over-all cost of production of the initial methyl bromide. This is particularly the case in the synthetic-fuels industry, where gasoline and fuel oil are synthesized from natural gas, coal, or shale rock. Alcohols and other

chemicals are produced as side products, and their sale is a big factor in determining *whether or not the synthetic fuel industry can compete with the production of gasoline from petroleum.*

3. Many organic reactions are made to take place *successfully only* by the application of high temperatures, high pressures, or suitable catalysts, and usually only with a combination of all three conditions. It requires special equipment to accommodate extremely high pressures and temperatures, which is too expensive for other than research laboratories. As a result industry is capable of carrying out many reactions which are not practical in the student laboratory. This will be observed frequently as the preparations of the various classes of compounds are taken up.

On the other hand, relatively small quantities are used in the laboratory, and usually the cost of the chemicals is not of primary concern. Of greater concern is the ease of separating any side products, the ease of removing the impurities, and the availability of starting materials. Naturally, other things being equal, one would choose the method that is the most efficient, i.e., gives the largest per cent yield.

Consequently, from the standpoint of over-all costs, feasibility of experimental conditions, and ease of isolation of pure products, the industrial and laboratory preparations will frequently be different.

On a commercial scale, the common alkanes are not produced synthetically but are isolated from natural gas and petroleum. Much more will be said in Section 2.8 about these natural resources. For the present it is sufficient to say that all the common alkanes are obtained from petroleum, and natural gas has the following approximate composition:

Constituent	*Per cent*
CH_4	80–90
C_2H_6	5–10
C_3H_8	3–5
C_4H_{10}	1–2
C_5—C_7	1–2

2.4 ALIPHATIC FREE RADICALS

Soon after it was realized that organic compounds contained atomic groupings or radicals that can be joined through a reaction such as the Wurtz reaction, attempts were made to isolate such radicals in the free state. Free radicals are highly reactive and quickly couple up with other free radicals or vigorously attack substances for an electron in order to form an electron pair. Finally, in 1929 Paneth was able to show the transitory existence of free methyl radicals by passing tetramethyllead, $Pb(CH_3)_4$, through a tube in a current of an inert gas, such as hydrogen or nitrogen, at low pressure.

The actual setup was more complex, but the essential features of Paneth's experiment were as follows. A tube was heated at a particular spot A, and at this spot a lead mirror was formed from the decomposition of the tetramethyllead (Figure 2.2). This spot was then allowed to cool, and another spot, B, nearer the source of the gas stream was heated. A new mirror formed at this second spot with simultaneous disappearance of the first lead mirror at A. It was concluded that methyl radicals from the decomposing tetramethyllead at spot B existed long enough to travel to the first lead mirror at A and convert the lead into gaseous $Pb(CH_3)_4$. If the mirror at A was more than a certain distance from the source of methyl radicals at B, the mirror was not removed, indicating that the methyl free radicals had decomposed before reaching A.

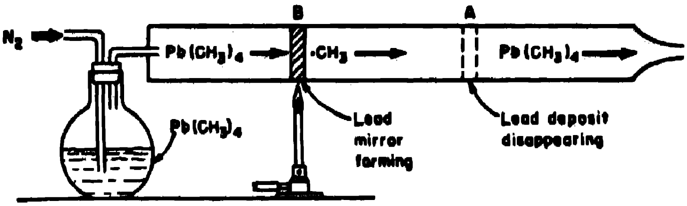


Fig. 2.2. Passage of tetramethyllead through tube.

From measurements of the rates of removal of mirrors, the velocity of the gas current, and the distance between spots, Paneth calculated the half-life of the methyl radical under his experimental conditions to be of the order of 0.006 seconds. This means that one-half the total amount of free methyl radicals will be decomposed in that length of time. His experiments inspired a widespread search for other aliphatic free radicals, and since then many have been found to exist with extremely short half-lives. Many reactions, however, take place through the transient formation of free radicals, as will be pointed out throughout this book. For reasons to be learned when they are discussed, it will be found that some free radicals, particularly aromatic free radicals, may be sufficiently stable to exist in solution or even in the solid state.

2.5 PROOF OF STRUCTURE

The question has probably occurred to the reader, how are specific structures assigned to molecules, particularly to isomers? For instance, two hydrocarbons are obtained from petroleum which, upon analysis and vapor density measurements, are found to have the molecular formula C_4H_{10}. One, *a*, has a boiling point of $-10°$ and the other, *b*, has a boiling point of $-0.6°$. Their other physical properties differ, too, such as their densities, refractive indexes, etc. But how are their structures determined? From the structural theory, based on a tetrahedral carbon atom and a valence of four for carbon and one for hydrogen, it is evident that only two alternatives are possible,

$CH_3—CH_2—CH_2—CH_3$ and $(CH_3)_3CH$. There remains the problem of assigning the correct structural formula to *a* and *b*, i.e., putting the correct formula on the label of each bottle.

There is only one bromoethane, and its structure is known (see Chapter 9). When it is treated with sodium metal it yields C_4H_{10}, b.p., −0.6° C., which has properties identical to those of *b* from petroleum. Since experience has shown that carbon chains do not rearrange under such experimental conditions, it is easy to decide that *b* has the straight-chain structure.

$$2CH_3—CH_2—Br + 2Na \rightarrow CH_3—CH_2—CH_2—CH_3 + 2NaBr$$

Isomer *a* must then be assigned the other possible structure, although its structure can also be determined by chemical reactions and similar reasoning.

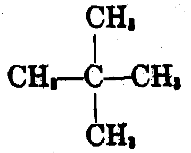
Either by synthesis from known substances, as above, or by orderly degradation of a molecule into substances of proved structure, the structures of all new organic compounds are determined. Originally progress was very slow because the structures of only a few compounds were already known for reference. In recent years much has been learned about relationships between the chemical constitution and the physical properties of molecules, such as color, absorption spectra, dipole moments, electron and X-ray diffractions, parachor, and many others. The combination of such physical methods with chemical methods can bring about a quick structure assignment, although sometimes for biological substances it may take years because of the complexity of their structures. Simple applications of some of these methods will be given throughout this book, particularly the phases of qualitative analysis and the use of derivatives.

2.6 PHYSICAL PROPERTIES OF ALKANES

The alkanes are typical homopolar (nonpolar) organic compounds whose intermolecular forces are of the van der Waals type (page 264). Such forces are weak, short-range, attractive forces, and the magnitude of the total intermolecular attractions depends on the extent to which the molecules can get close to each other. Thus, linear molecules can line up with a greater proportion of their surfaces in close contact than can spherical molecules. Accordingly, the normal alkanes have slightly higher boiling points than their branched chain isomers. For example, the boiling points of *n*-pentane and neopentane are 36.1° and 9.5°, respectively.

$$CH_3—CH_2—CH_2—CH_2—CH_3$$

n-Pentane, b.p. = 36.1°



$$CH_3—\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}—CH_3$$

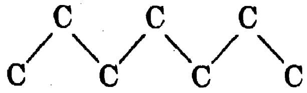
Neopentane, b.p. = 9.5°

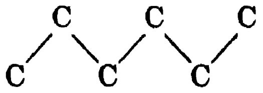
It will be observed that for the various classes of compounds, melting points, boiling points, viscosities, and densities rise with increasing molecular weights (see Section 2.8). This is illustrated in the case of melting and boiling points for the *n*-alkanes in Table 2.2 and Figure 2.3. It can be seen that at

TABLE 2.2. PHYSICAL CONSTANTS OF SOME NORMAL SATURATED HYDROCARBONS

Name	Molecular Formula	Melting Point	Boiling Point	Sp. Gr. (liq.)
Methane	CH_4	−183	−162	0.424
Ethane	C_2H_6	−172	−89	.546
Propane	C_3H_8	−187	−42	.582
n-Butane	C_4H_{10}	−138	0	.579
n-Pentane	C_5H_{12}	−130	36	.626
n-Hexane	C_6H_{14}	−95	69	.659
n-Heptane	C_7H_{16}	−91	98	.684
n-Octane	C_8H_{18}	−57	126	.703
n-Nonane	C_9H_{20}	−54	151	.718
n-Decane	$C_{10}H_{22}$	−30	174	.730
n-Undecane	$C_{11}H_{24}$	−26	196	.740
n-Dodecane	$C_{12}H_{26}$	−10	216	.749
n-Tridecane	$C_{13}H_{28}$	−6	235	.757
n-Tetradecane	$C_{14}H_{30}$	6	254	.764
n-Pentadecane	$C_{15}H_{32}$	10	271	.769
n-Hexadecane	$C_{16}H_{34}$	18	287	.775
n-Heptadecane	$C_{17}H_{36}$	22	302	.777
n-Octadecane	$C_{18}H_{38}$	28	316	.777
n-Nonadecane	$C_{19}H_{40}$	32	330	.778
n-Eicosane	$C_{20}H_{42}$	36	343	.778
n-Heneicosane	$C_{21}H_{44}$	40	356	.778
n-Docosane	$C_{22}H_{46}$	44	369	.779
n-Tricosane	$C_{23}H_{48}$	48	380	.780
n-Triacontane	$C_{30}H_{62}$	66	450	.806
n-Tetracontane	$C_{40}H_{82}$	81	525	.817

room temperature, 25°, C_1—C_4 are gases, C_5—C_{17} are liquids, and the rest are solids. The zigzag shape of the melting-point curve is probably due to the fact that the alkanes with an odd number of carbon atoms have their end carbon atoms on the same side of the molecule and the even-numbered carbon atom alkanes have their end carbon atoms on opposite sides of the molecules.





Apparently the alkanes having an even number of atoms can pack so as to permit greater intermolecular attraction and hence have slightly higher melting points.

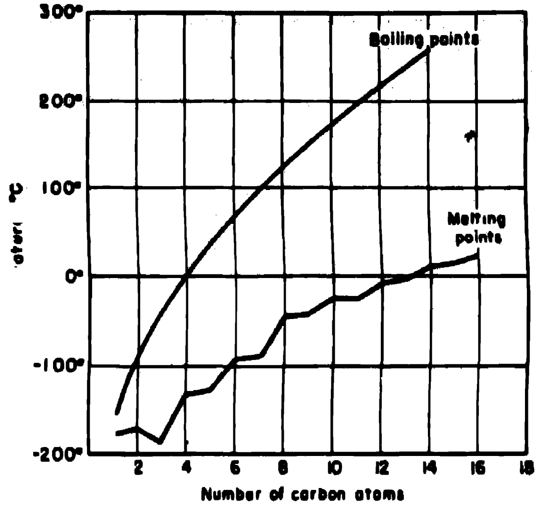


Fig. 2.3. Boiling-point and melting-point curves for the *n*-alkanes.

2.7 CHEMICAL PROPERTIES OF ALKANES

It was shown in Section 1.2 that organic reactions take place by the attack on an organic molecule by a free radical or a polar reagent. Most of the common organic reactions involve *electrophilic* (electron-seeking, such as cations) or *nucleophilic* (nucleus-seeking, such as anions and bases) reagents, but alkanes are inert toward these types of reagents. They are, for example, unaffected by chemical oxidizing and reducing agents, concentrated alkali, or concentrated acids at moderate temperatures. This fact led to their being called *paraffins* or compounds of "little affinity." They do, however, react readily with free radicals. Therefore, to bring about a smooth reaction under mild conditions, either illumination or peroxides are employed to initiate the formation of free radicals. Unfortunately this can be done with very few useful reactions, one of which is halogenation. The alternative is to use a very high temperature where it is probable that free radicals are produced by thermal decomposition. It is under such drastic conditions that several of the reactions of alkanes are conducted. Some of these may now be discussed.

a. Oxidation. All hydrocarbons are combustible and in the presence of excess air or oxygen, the carbon is converted into carbon dioxide and the hydrogen into water. For the alkanes, this may be expressed

$$C_nH_{2n+2} + \left(\frac{3n+1}{2}\right) O_2 \rightarrow n\,CO_2 + (n+1)\,H_2O + \text{heat}$$

In an insufficient supply of oxygen, the carbon may be oxidized only to elemental carbon or carbon monoxide. This is the reason exhaust fumes from automobiles are so deadly; they contain a high concentration of the toxic gas, carbon monoxide. Also, when the air vent of the Bunsen burner is closed to shut off the air, a coat of soot (carbon) forms on the bottom of the vessel being heated. The flame is not very hot and the gas is burned largely to carbon which condenses on the cooler surface. When the vent is opened, a hotter flame results and it burns the soot to carbon dioxide, and thereupon the black coating disappears.

Although *combustion* is oxidation, the term *combustion* is restricted to rapid oxidation by oxygen with the liberation of heat and light, and is not of particular chemical significance.[1] It is, of course, of importance from the standpoint of hydrocarbons serving as combustion fuels in furnaces. In this respect, methane has the highest heat of combustion per gram.

In spite of the fact that all hydrocarbons are combustible, the alkanes are characterized by being extremely resistant to chemical oxidation. For instance, potassium permanganate is a strong oxidizing agent capable of oxidizing most classes of organic substances, and for this reason it is chosen as the standard reagent for testing the oxidizability of organic substances. Alkanes are one of the few types of substances which are inert toward $KMnO_4$.

Commercially alkanes may be catalytically oxidized by air at high temperatures to produce oxygenated products. The direct oxidation of the lower saturated hydrocarbons expanded rapidly in the postwar years. A typical product distribution is given below.

$$C_4H_{10} \xrightarrow{O_2} CH_3OH + HCHO + CH_3CHO + CH_3COCH_3 + \text{other}$$

	methyl alcohol	formaldehyde	acetaldehyde	acetone	aldehydes, acids, and alcohols
100 lb.	19 lb.	15.2 lb.	19.6 lb.	7 lb.	12.9 lb.

Butane oxidation products

An indirect route consists in burning the alkanes to carbon or carbon monoxide and then hydrogenating these to other hydrocarbons and oxygenated compounds. This is the basis of producing synthetic fuels from natural gas, or from anything which can be burned to carbon monoxide. This is discussed in Section 2.8.

When hydrocarbons, saturated or unsaturated, are mixed with air within certain proportions, the mixtures will explode violently upon ignition. This

---

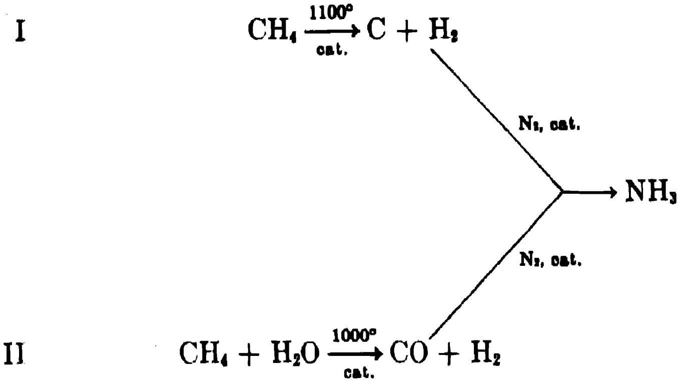
[1] There are certain oxidations not involving oxygen which liberate light and this phenomenon is referred to as *chemiluminescence*. For example, when hydrogen peroxide is added to a solution of formaldehyde in alkaline pyrogallol, light is emitted with the evolution of hydrogen gas.

$$2H_2CO + H_2O_2 \rightarrow 2HCO_2H + H_2 + \text{light}$$

Another widely used reaction is the oxidation of luminol with potassium ferricyanide.—E. H. Huntress, L. N. Stanley, and A. S. Parker, *J. Chem. Educ.* **11**, 142 (1934).

is the cause of many explosions in coal mines, where methane is known as *firedamp*.

Finally, when hydrocarbons are heated to high temperatures in the presence of metallic catalysts, they may lose hydrogen or the carbon skeletons may undergo fission. This process is called *cracking* and will be discussed in Section 2.8. When a hydrocarbon loses hydrogen, it is effectively being oxidized. Occasionally such a process is carried out commercially, as for example in the production of ethylene, $CH_2{=}CH_2$, from ethane, or the production of hydrogen itself from methane. Surprisingly, the petrochemical industry is one of the largest producers of ammonia through its production of hydrogen from natural gas. Two different processes are used:



$$\text{I} \qquad CH_4 \xrightarrow[\text{cat.}]{1100^\circ} C + H_2$$

$$\text{II} \qquad CH_4 + H_2O \xrightarrow[\text{cat.}]{1000^\circ} CO + H_2$$

b. Sulfonation. Alkanes react with fuming sulfuric acid at elevated temperatures to produce alkanesulfonic acids.

$$R{-}H + HOSO_3H \xrightarrow{400^\circ} R{-}SO_3H + HOH \qquad \textit{Tert.} > \textit{Sec.} > \textit{Prim.}$$

Tertiary carbons react faster than secondary carbons which react faster than primary carbons. The reaction is not a useful one, since such drastic conditions must be used. Fortunately, the alkanesulfonic acids can be produced more conveniently by the reaction sequence,

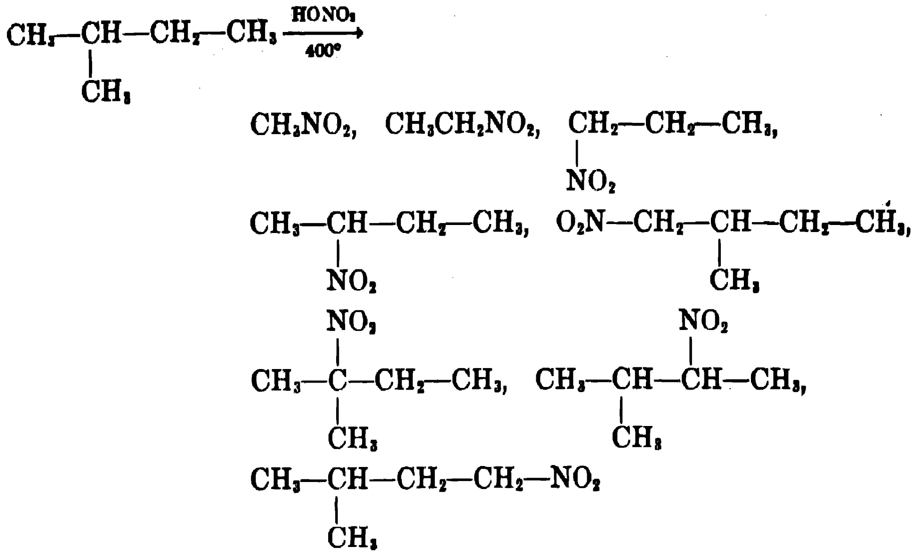
$$\begin{aligned} RH + SO_2Cl_2 &\xrightarrow{\substack{\text{illumination}\\ \text{or peroxide}}} RSO_2Cl + HCl \\ &\qquad\quad \xrightarrow{H_2O} RSO_3H + HCl \end{aligned}$$

in which the first step takes place by a free radical mechanism.

c. Nitration. Nitration of alkanes, too, is difficult and requires high temperatures.

$$R{-}H + HONO_2 \xrightarrow{400^\circ} R{-}NO_2 + HOH \qquad \textit{Tert.} > \textit{Sec.} > \textit{Prim.}$$

Practically only mononitroalkanes are produced. The reaction has the drawback that many fission products are produced, and alkyl groups may even be replaced by nitro groups. For example, nitration of 2-methylbutane yields the following products:



$$CH_3-\underset{\underset{CH_3}{|}}{CH}-CH_2-CH_3 \xrightarrow[400^\circ]{HONO_2}$$

$$CH_3NO_2,\quad CH_3CH_2NO_2,\quad \underset{\underset{NO_2}{|}}{CH_2}-CH_2-CH_3,$$

$$CH_3-\underset{\underset{NO_2}{|}}{CH}-CH_2-CH_3,\quad O_2N-CH_2-\underset{\underset{CH_3}{|}}{CH}-CH_2-CH_3,$$

$$CH_3-\overset{\overset{NO_2}{|}}{\underset{\underset{CH_3}{|}}{C}}-CH_2-CH_3,\quad CH_3-\underset{\underset{CH_3}{|}}{CH}-\overset{\overset{NO_2}{|}}{CH}-CH_3,$$

$$CH_3-\underset{\underset{CH_3}{|}}{CH}-CH_2-CH_2-NO_2$$

The higher the temperature employed, the greater is the yield of fission products. Various oxidation by-products are produced, and usually it is profitable to isolate them.

Thus, with so many substances being produced, the synthesis of nitroalkanes by nitration of alkanes is ordinarily not done in the laboratory. Instead, methods are used as discussed in Section 16.4.

d. Halogenation. The general equation is simply

$$R-H + X_2 \xrightarrow{h\nu,\,\Delta} R-X + HX \qquad \textit{Tert.} > \textit{Sec.} > \textit{Prim.}$$
$$F_2 \gg Cl_2 > Br_2 > I_2$$

where X_2 is a molecular halogen, R—X is an alkyl halide, $h\nu$ is the symbol for radiation (usually sunlight or artificial illumination), and Δ is used to indicate heat. X_2 may be any of the four halogens—F_2, Cl_2, Br_2, or I_2—but in this reaction it is normally restricted to just Cl_2 and Br_2. In the case of fluorine, the heat of reaction (cf. below) is greater than the C—C bond energy, with the result that C—C bonds are broken during fluorination. Because of the strong reducing power of HI, the reaction with iodine is reversible, with the equilibrium lying on the left side of the equation. Hence, direct fluorination and iodination are rarely feasible.

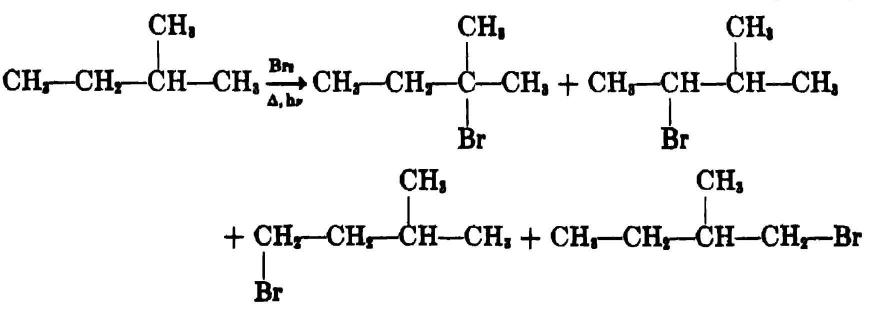
When methane and chlorine react to produce methyl chloride plus hydrogen chloride, a C—H bond and a Cl—Cl bond are broken, and a C—Cl and an H—Cl bond are formed. Energy must be supplied initially to break the first two bonds (referred to as their *bond strengths* or *bond energies*) and a certain quantity of energy is given up when the new bonds are formed. With chlorination, the over-all change or the heat of reaction is exothermic. From the respective energy changes below, it can be seen that fluorination, chlorination, and bromination are exothermic, whereas iodination is endothermic. The heat from fluorinations frequently ignites the hydrocarbon. Hence, only chlorination and bromination are used for preparative purposes.

$$\begin{array}{llllll}
C-H & + F-F & \rightarrow C-F & + H-F & \Delta H = & -104.8\ \text{kcal} \\
98.2 & 50 & 112 & 141 & & \\
C-H & + Cl-Cl & \rightarrow C-Cl & + H-Cl & \Delta H = & -24.8\ \text{kcal} \\
98.2 & 57.1 & 78 & 102.1 & & \\
C-H & + Br-Br & \rightarrow C-Br & + H-Br & \Delta H = & -7.9\ \text{kcal} \\
98.2 & 45.4 & 64.8 & 86.7 & & \\
C-H & + I-I & \rightarrow C-I & + H-I & \Delta H = & +6.6\ \text{kcal} \\
98.2 & 35.6 & 56.6 & 70.6 & &
\end{array}$$

The first few alkanes react very readily with chlorine. For example, methane is chlorinated rapidly in the dark and explosively in sunlight. As a general procedure, however, chlorination and bromination of the alkanes require heat and illumination for a successful reaction (see page 18 for mechanism).

As stated in Section 1.2, reaction does not stop after monohalogenation, nor does reaction take place with the same carbon atoms in all molecules of a particular substance. That is, bromination of propane can produce two monobromopropanes (1-bromopropane and 2-bromopropane), four dibromopropanes, four tribromopropanes, etc. Thus, many products will be produced and unless a compound is such as to give predominantly one-halogenation product, the reaction is not used in the laboratory. If a desired alkyl halide is sought, it is prepared by one of several other methods or bought commercially. Industry, on the other hand, does not object strongly to several products, because the reaction mixtures can be fractionated conveniently in the large distillation columns and the by-products can be shelved to build up a stock of various halogenated alkanes.

Although halogenation of alkanes and their derivatives gives several products from one compound, the substitution is not completely random. When a halogen atom attacks the organic molecule, it can most easily remove a hydrogen atom from a tertiary carbon and least easily from a primary



$$CH_3-CH_2-\overset{\overset{CH_3}{|}}{C}H-CH_3 \xrightarrow[\Delta,\,h\nu]{Br_2} CH_3-CH_2-\underset{\underset{Br}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_3 + CH_3-\underset{\underset{Br}{|}}{C}H-\overset{\overset{CH_3}{|}}{C}H-CH_3$$

$$+ \underset{\underset{Br}{|}}{C}H_2-CH_2-\overset{\overset{CH_3}{|}}{C}H-CH_3 + CH_3-CH_2-\overset{\overset{CH_3}{|}}{C}H-CH_2-Br$$

carbon atom. Thus, among the monobromination products from isopentane, the 2-bromo-2-methylbutane would be produced in the largest amount. Also, substituents in an alkane molecule influence the reactivity of various C—H bonds. For example, the percentages of monochlorination products obtained in the chlorination of substituted propanes are as follows: Z represents the substituent indicated below and the figures denote the relative amounts of chlorination occurring at the respective carbon atoms. For illustration, chlorination of 1-chlorobutane (Z = CH_2Cl) gives 24% of 1,2-dichlorobutane, 51% of 1,3-dichlorobutane, and 25% of 1,4-dichlorobutane.

C—	—C—	—C	Z
↑	↑	↑	
		50	C_6H_5
20	40	40	CH_3
25	51	24	CH_2Cl
29	*46*	*25*	$OCOCH_3$
38	*49*	*13*	*$CHCl_2$*
41	46	*13*	$SiCl_3$
45	45	10	COOH
45	45	10	Cl
47	50	3	$OCOCCl_3$
48	49	3	COCl
50	42	8	CCl_3
55	45	0	CF_3

The descending order of the groups closely parallels their electronegativities and it can be seen that there is a drift in the position of chlorination away from the substituent with increasing electronegativity of the substituent.

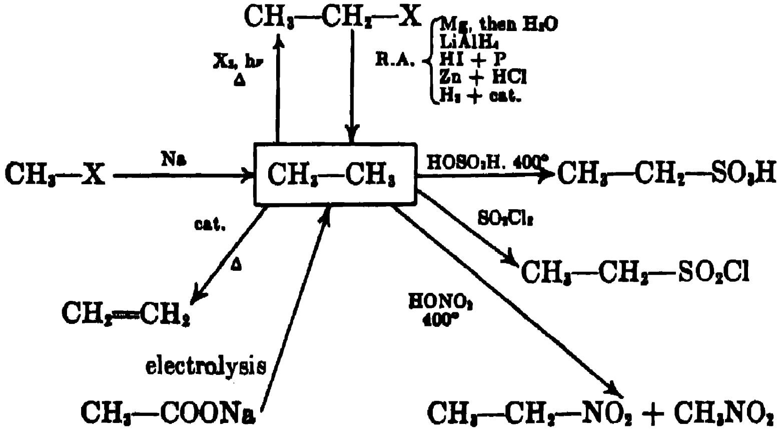


Fig. 2.4. Characteristic reaction chart for alkanes.

2.8 HOMOLOGY

Owing to the formation of carbon chains, there is a certain relationship between the structures of the members of each family of compounds. For illustration, the structures of ethane, propane, *n*-butane, etc., are obtained from methane by the successive insertion of CH_2 groups between the end carbon and hydrogen atoms.

CH_3-H
CH_3-CH_2-H
$CH_3-CH_2-CH_2-H$
$CH_3-CH_2-CH_2-CH_2-H$

The series can be represented by the general structure, $CH_3-(CH_2)_n-H$. Similarly, one may start with methyl alcohol or methyl chloride and successively place a CH_2 group between the end carbon atoms and the substituents to form the family of alcohols, or the family of *n*-alkyl chlorides.

CH_3-OH	CH_3-Cl
CH_3-CH_2-OH	CH_3-CH_2-Cl
$CH_3-CH_2-CH_2-OH$	$CH_3-CH_2-CH_2-Cl$
$CH_3-(CH_2)_n-OH$	$CH_3-(CH_2)_n-Cl$

$CH_3-CHOH-CH_3$
$CH_3-CH_2-CHOH-CH_3$
$CH_3-CH_2-CH_2-CHOH-CH_3$
$CH_3-(CH_2)_n-CHOH-CH_3$

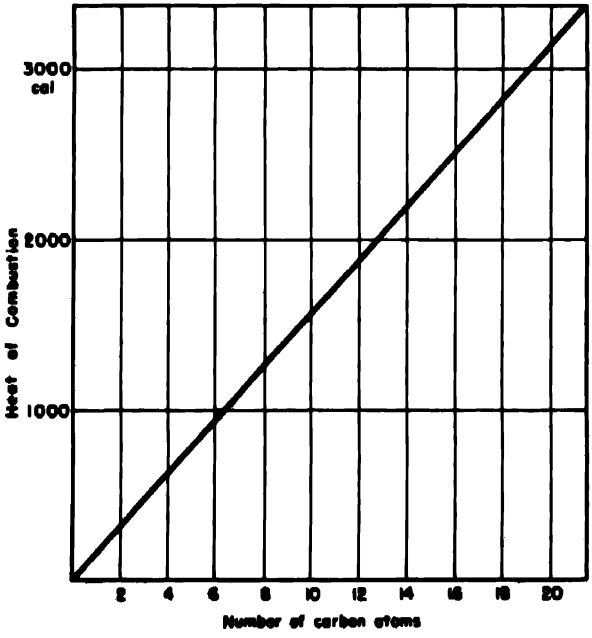


Fig. 2.5. Plot of the heat of combustion vs. chain length of the *n*-alkanes.

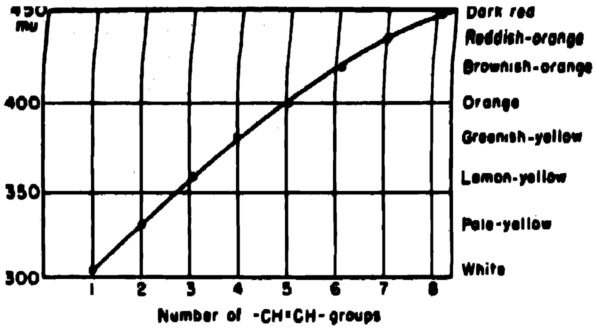


Fig. 2.6. Graph of the color (wavelength of light absorption) vs. number of —CH=CH— bonds in the diphenylpolyenes, C_6H_5— $(CH{=}CH)_n$—C_6H_5.

The last series shows that the repeated structural unit need not necessarily come at the end of the chain. Each of these related series, or families, is called a *homologous series* (Gr. *homos*, the same, and *logos*, word, speech); i.e., a series of compounds in which any two consecutive members differ by a structural unit that is common for the series. The members of a homologous series are called *homologs*, and the phenomenon is referred to as *homology*. The most common structural unit in forming homologous series is the *methylene group*, CH_2, but other structural units are possible. For instance, other homologous series are CH_3—$(CH{=}CH)_n$—COOH and Cl—$(CH{=}CH)_n$—Br where the common structural unit which builds up the series is the —CH=CH— group.

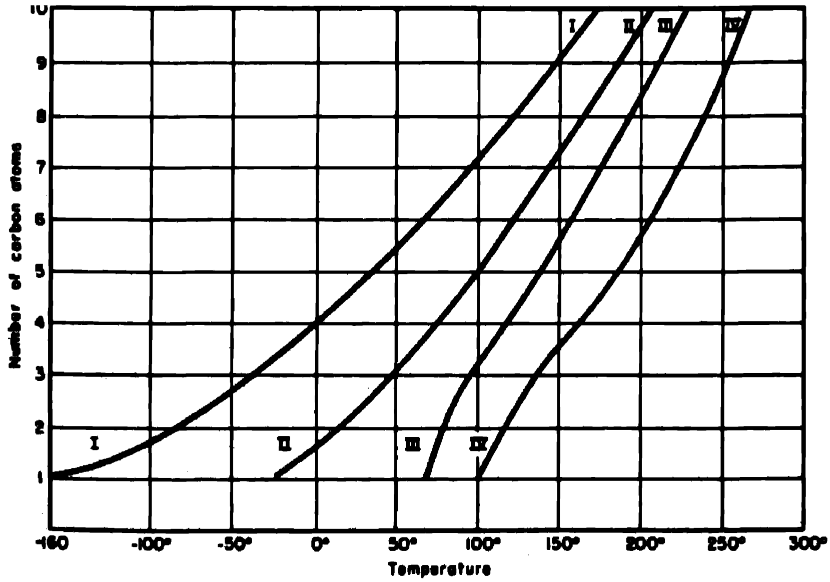


Fig. 2.7. Boiling-point curves for the homologous series: I, *n*-alkanes, II, *n*-aldehydes $(H—(CH_2)_n—CHO)$, III, *n*-alcohols $(H—(CH_2)_n—CH_2OH)$, IV, *n*-carboxylic acids $(H—(CH_2)_n—COOH)$.

Homology serves a very useful function. For illustration, it is usually found that a regular curve is obtained when any physical property of a homologous series is plotted against the positions of the members in the series. For example, a smooth curve is obtained when the boiling points of the first ten *n*-alkanes are plotted against the number of carbon atoms in the molecules, as seen in Figure 2.3. Should there be an *n*-alkane whose boiling point is not known, its boiling point could be estimated with high reliability by extrapolation on the graph. In a similar fashion, the viscosity, melting point, density, color, index of refraction, or other physical property can be plotted against the chain length of a homologous series. Not always is a straight line obtained, but normally one gets a smooth curve from which the values for missing members in a series may be estimated by interpolation or extrapolation. Several examples are shown in Figures 2.5, 2.6, and 2.7.

2.9 THE STORY OF PETROLEUM AND NATURAL GAS[2]

Over one-half the value of the entire chemical industry originates from petroleum and natural gas, and also, over 50 per cent of the total U.S. energy comes from these materials. Chemicals which stem from petroleum or natural gas are called *petrochemicals*, and the industry has had a phenomenal rate of growth. For illustration, the average yearly increase for this industry has been 15 per cent, as compared to 10 per cent for the chemical industry as a whole and 3 per cent for all industries. Because of the importance of the petroleum and natural-gas industries, this section gives an extensive description of these industries. Many of the terms mentioned throughout this section and most of the reactions given in the latter portion will not and need not be understood at this time. They are included merely for organization, and reference will be made to this section frequently in the course, at which times it will be comprehensible.

In Biblical times, petroleum was used for coating the bodies of boats and the walls of temples and palaces, as an illuminant, for embalming, and for other purposes. A century ago a rubbing ointment or an intestinal lubricant was made from petroleum which North American Indian medicine men, frontier housewives, and patent-medicine barkers obtained from so-called "natural oil" taken from surface seepages. A half-century ago kerosene was the chief derivative of petroleum, being used as fuel for lamps. A quarter-century ago gasoline was the "gem" of the petroleum industry. Today petroleum is a "treasure chest" for industrial chemicals, although coal shows promise of becoming an even greater storehouse of chemicals. From petroleum are derived medicines, insecticides, rubber, perfumes, plastics, explosives, motor fuel, and almost any carbon-containing substance mentionable.

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[2] The American Petroleum Institute and the American Gas Association, both in New York City, will supply teachers with a host of free descriptive materials, consisting of booklets, charts, filmstrips, and other teaching aids to provide information and stimulate interest in petroleum and natural gas.

A comprehensive discussion of petroleum may be found in the three volumes of *The Chemistry of Petroleum Hydrocarbons*, edited by B. T. Brooks, C. E. Boord, S. S. Kurtz, and L. Schmerling, Reinhold Publishing Corporation, New York, 1954–55.

a. *Origin.* *Buried in the earth are vast amounts of carbonaceous* substances, the most common being petroleum, natural gas, coal, and diamonds. It is believed that animal and plant remains, after being embedded in the earth at elevated temperatures for millions of years and subjected to great pressures by gas evolution plus superimposed layers of silt, sand, and rock strata, were changed into carbon-containing residues. Depending upon the conditions, the chemically bound nitrogen, sulfur, oxygen, hydrogen, and other elements in the organisms were converted into mineral matter or inorganic gases, while most of the carbon was transformed into carbonaceous gases (natural gas), liquids (petroleum), and solids (coal, shale, tar sand, diamond, etc.). These solids contain varying percentages of carbon, ranging from about 10 per cent in shale, peat, and tar sands, to 35 per cent in lignite, 65 per cent in bituminous coal, 85 per cent in anthracite coal, and up to 100 per cent in diamonds.

The leading petroleum-producing states are Texas, California, Kansas, Louisiana, Oklahoma, Wyoming, and New Mexico. Other rich regions are Mexico, Dutch East Indies, Arabia, and Russia. The United States produces 30 per cent and uses 50 per cent of the world's supply of petroleum. Petroleum constitutes about 0.9 per cent of the total U.S. fuel resources, natural gas about 0.7, shale about 3.4, and coal about 95 per cent.

b. Oil wells. In oil-bearing areas usually some brine, oil, natural gas, and sand in varying proportions are present. The problem is to locate the oil or gas and recover as much of it as possible. James M. Williams of Hamilton, Ontario, is reported to have dug the first successful, commercial oil well in North America in 1857. The first oil well in the United States was drilled by "Colonel" Edwin L. Drake on Oil Creek, now Titusville, Pennsylvania, in 1859. This well was 69 feet deep and produced 30 barrels of oil a day at a cost of 20 dollars per barrel. Now the United States produces over 7 million barrels per day from wells that extend down over 15,000 feet. The proved reserves of petroleum, now over 29 billion barrels, have always increased in spite of the increased consumption.

New oil- and gas-bearing areas are located today with the aid of scientific equipment. Surface prospectors study physical properties of the earth, such as the force of gravity, magnetism, hardness, or radioactivity, from which certain values indicate the probable locality of oil or gas. A gravity meter measures the variation in gravity caused by changes in rocky formation. A magnetic susceptibility measuring device, nicknamed a "doodle bug" or a "flying eye," detects highly magnetic rock. The electrical conductance of oil is poor, and therefore a low electrical conductivity between two poles may reveal an oil-bearing spot. Seismographs record shock waves sent downward by explod-

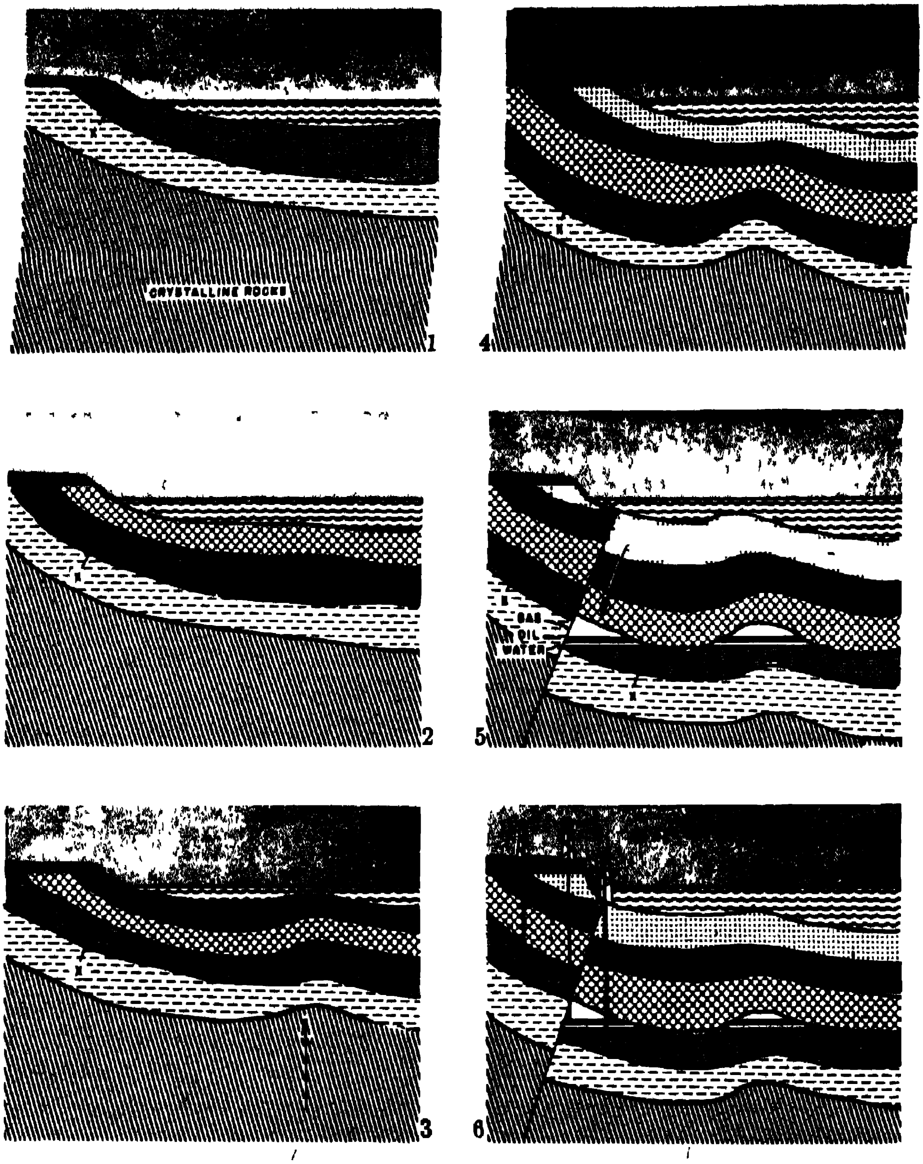


Fig. 2.8. *Probable scheme of development of gas and oil wells*

1. Sea ooze trapped a mass of plant and animal remains from land and ocean in a firm layer.
2. The new silt on top buried the stratum and created pressure and heat on the bits of matter.
3. Bacteria or other agents turned these into carbonaceous residues. A tremor folded the earth's crust, which one can imitate by bending the leaves of an ordinary tablet.
4. Water seeped through the porous rock. The less dense oil and gas rose to the top in the stratum.
5. The rock layers cracked and slipped past one another, and an impervious layer sealed the gas and oil in the fault.
6. Today man digs up this chemical treasure. A well may hit either dry area, gas, oil, or water, or any combination of these.

ing dynamite and reflected back from hard surfaces to indicate rock strata, perhaps pocketing oil. Since hydrogen atoms are good neutron stoppers and oil has a high hydrogen content, neutron bombardment has been used to detect oil.

By means of such measuring devices, the chance of hitting oil or gas when drilling a new well is one out of eight these days, whereas the nontechnical "wildcat hunches" and use of divining rods were correct less than once out of 30 times. With odds of eight to one that a hole will be dry, it still holds that "oil is where you find it." It is expensive to drill holes; the average cost in 1954 was $123,000 per well.

In recent years considerable attention has been given to oil prospecting beneath the coastal waters of the Gulf of Mexico and off the California coast. These continental shelves, about 600 feet or less beneath the water level, show promise of having extensive oil deposits. In most cases wells are drilled from anchored platforms over the water.

In 1901 the first oil well in the Gold Coast district roared into being, and until its tremendous pressure could be capped, it shot an estimated 75,000 to 100,000 barrels of oil a day 200 feet into the air. Gushers are a thing of the past, for now wells are never allowed to flow wide open. In this connection, there are two major developments in petroleum engineering designed to increase the efficiency of oil recovery from wells. One is *cycling*, whereby the "wet" gas from an oil well is treated for the removal of natural gasoline and other liquefiable contents, and then recompressed and returned underground through injection wells to maintain pressure in oil-bearing formations. In the second technique, called *flooding*, water is pumped at high pressure into chosen wells, filling voids left by withdrawn oil and gas and driving the remaining oil into producing wells. As a result of these and other modern practices, about 50 per cent of the petroleum in an oil field can be extracted, whereas only 25 per cent was recoverable years ago. In 1865 the average life of an oil well was about 2 years; in 1885 it grew to 7 years; it was 21 years in 1931; and today the average life-span is about 30 years.

c. Description. Petroleum got its name from the Latin words, *petra*, rock, and *oleum*, oil. It consists of a large number of hydrocarbons dissolved in one another along with various sulfur-, oxygen-, and nitrogen-containing substances. The composition and appearance differ, depending upon the location of the well, with the color ranging from yellow through red to black. It is classified as *paraffin-base* if the residue after removal of the volatile fractions contains mostly paraffin wax, and as *asphalt-base* if this residue contains mostly asphaltics. The paraffin base contains a larger percentage of gasoline, but there is less of it.

d. Refining. *Natural gas* is a mixture of hydrocarbon and nonhydrocarbon gases.

The Belgian physician Jan B. van Helmont (1579–1644) was the first writer to use the word "gas," and it is said that the name came from the German word *geist* and the Old English word *gast*, both meaning ghost. As early as 1802, the streets of Genoa, Italy, were lighted by gas. The first American gas well was brought in at Fredonia, N.Y., in 1821. It was 27 feet deep and the gas, piped through hollowed logs, was used to illuminate the town.

The several hydrocarbon components of gas can be separated from one another by fractional distillation. Some nonhydrocarbon gases are separated by extraction. This fractionation is diagrammed in Figure 2.9.

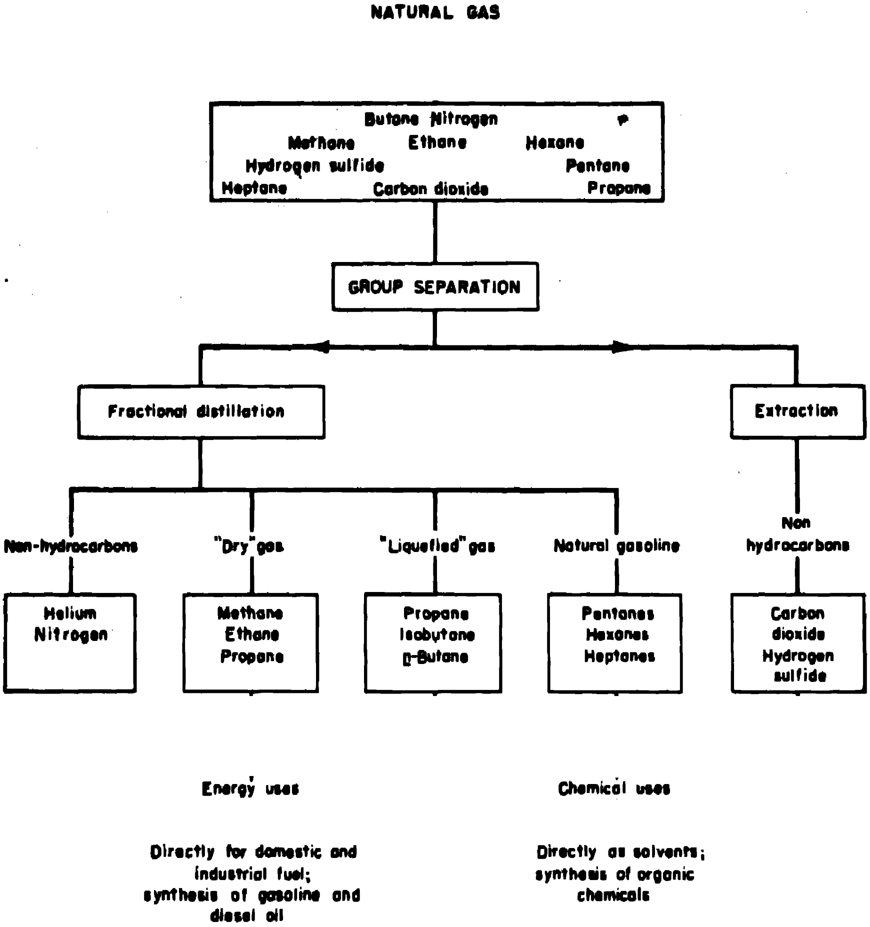


Fig. 2.9. Flowsheet for the fractionation of natural gas.

Crude petroleum is piped to the refinery from a well and fractionated by distillation into several volatile fractions. Normally, tall bubble-cap fractionating columns are used, and several broad fractions can be withdrawn at various levels. A common practice is to stop the distillation after the kerosene fraction, and the residue, called *reduced crude*, is used for fuel, lubrication, or for cracking stock. A typical fractionation of petroleum is given in Table 2.3. An extremely meticulous fractionation of one grade of petroleum yielded 146 different hydrocarbons, including paraffins and carbocyclic hydrocarbons.

e. Treatment and uses of fractions.

Gaseous hydrocarbons: These are used as follows:

1. Gaseous hydrocarbons serve as fuel in furnaces and internal combustion engines. The propane and butane may be separated and compressed into liquid form which can then be transported in steel cylinders. The

TABLE 2.3. TYPICAL FRACTIONATION OF PETROLEUM

Name	Composition	Approximate Percentage	Boiling Range
Gaseous hydrocarbons	C_1—C_4	2	
Petroleum ether	C_5—C_6	2	20–60
Ligroin	C_6—C_7		60–100
Gasoline	C_7—C_{12}	32	70–200
Kerosene	C_{12}—C_{15}	18	200–275
Gas oil (diesel fuels)	C_{15}—C_{18}	20	Above 275
Lubricating oil and waxes	C_{16}—C_{24}		Not distilled
Coke or asphalt			Residue

bottled gas, called LPG (Liquid Propane Gas) reverts to its gaseous state when released from pressure. Many tractors, buses, and even taxicabs now use LPG for fuel. Chicago has over 1000 of its buses running on LPG, a fact which offers the advantage of producing less exhaust fumes. To take care of the varying seasonal demand for LPG, it is stored in deep underground caverns cut out of thick salt formations.

2. They are alkylated to produce gasoline (see Section 3.4d).
3. They are burned to form lampblack for tires, inks, etc.
4. They are used for chemical synthesis of tetraethyllead, alkenes (see Section 3.2b), and other products.
5. Methane is now the largest source of hydrogen (for ammonia synthesis), produced as indicated on page 66.

Petroleum ether and ligroin:

Petroleum ether and ligroin are used as solvents for varnish, perfumes, dry cleaning, and rubber.

Gasoline:

As initially obtained by distillation, the product is called *straight-run* gasoline and is of low octane rating. This is refined to remove (1) unsaturated hydrocarbons which form gums upon standing; (2) sulfur compounds which reduce antiknock effect of tetraethyllead, have unpleasant odors, and are toxic; and (3) aromatics and naphthenes (cycloalkanes). After this refinement, controlled amounts of substances are added for specific purposes, such as aromatics to raise octane ratings and ethylene bromide to convert the lead oxide (produced from tetraethyllead in the fuel) to volatile lead bromide, which then passes out with the exhaust gases. Thus, gasolines today are blends of C_5—C_9 alkanes mixed with additives to reduce knocking, lengthen exhaust-valve life, diminish oxidation, inhibit rust formation, prevent carburetor icing, and suppress spark-plug fouling and preignition. Typical concentrations of gasoline additives in commercial use are shown in Table 2.4.

TABLE 2.4. TYPICAL GASOLINE ADDITIVES IN COMMERCIAL USE

Type	*Concentration* (ppm. by wt.)
Dye	5
Antioxidant	20
Metal deactivator	4
Antirust	20
Anti-icing	11,000
Detergent	2500
Lubricant	2500
Deposit modifier	300
Antiknock fluid	2900

Over two-thirds of all motor vehicles in the world are in the United States. Consuming 50 billion gallons of gasoline annually, the United States uses 28 times per person more than the rest of the world, California being the largest consumer. Big four-engined planes take over 5000 gallons of gasoline at a fueling and burn it up at a rate of 600 gallons an hour. This amount of gasoline could run the average car around the world three times.

When the automobile became a major part of the American scene, there was an urgent need for a dependable method of evaluating gasolines. After considerable experimentation, the *octane scale* was developed. As such, the octane number of a fuel is the per cent of *Isooctane* in a mixture of Isooctane plus *n*-heptane that gives the same knock properties as the sample fuel. Isooctane is a trade name for 2,2,4-trimethylpentane, normally made by alkylating isobutylene with isobutane (see page 110).

Preignition of fuel in the cylinder ahead of the flame is called *knocking*. When a fuel burns, ignited by the spark plug, the rapidly expanding combustion gases compress the remaining unburned fuel and raise its temperature. If the temperature and pressure reach a certain critical value, depending on that particular fuel, the remainder of the fuel explodes spontaneously or is ignited by glowing deposits. When this occurs, the molecules strike the cylinder and piston surfaces with fantastic velocities and cause the cylinder structure to vibrate; this is heard as the familiar ping when pulling up a steep grade or attempting to accelerate the car rapidly. Also, it heats up the combustion-chamber parts. Thus, much of the fuel energy normally converted into power is dissipated as heat and mechanical energy. The situation is analogous to trying to move a piano. One would not run and bump into the piano to move it, but rather would get close and push against it steadily. Similarly, a steady, orderly combustion of gas in the cylinder generates the greatest amount of power. Branched-chain hydrocarbons have less tendency to knock than straight-chain hydrocarbons. Catalysts such as tetraethyllead greatly reduce knocking and, in addition, catalyze a complete combustion of fuel to gaseous products, which decreases carbon deposits. Tetraethyllead in the amount of about 2–4 ml per gallon of fuel usually improves a fuel by 2–3 octane numbers. Some highly branched-chain hydrocarbons have high octane ratings: for instance, triptane, 2,2,3-trimethylbutane, has an octane number of 116. Premium gas runs about 98 octane and regular gas about 95, and compression ratios average around 9 to 1.

Compression ratio is a term that indicates how much a given engine compresses its fuel—a mixture of gasoline vapor and air—in its cylinders before igniting it. The greater the compression before the fuel is fired by the spark plug, the more power obtainable from a gallon of gasoline, but the more the fuel tends to knock. Hence a compromise is reached. As better fuels are produced, higher compression ratios are used to give higher efficiencies. For example, two 1950 Cadillacs compared the pickup from 10 mi/hr in the same time interval using 1925 and 1950 gasolines. The 1925 gas pushed its car 780 ft while the car with 1950 gas went 1170 ft. Also, two 1950 Oldsmobiles, each with 0.1 gal of gas, one with 1925 gas and one with 1950 gas, averaged 22.5 mi/gal with the latter and 15.1 mi/gal with the 1925 gas.

Diesel engines differ from gasoline engines in that the mixture of fuel and air is allowed to ignite spontaneously by the high temperature generated during the compression of the fuel instead of using a spark. A high-compression ratio of 14–17 to 1 is used, and for these engines, straight-chain hydrocarbons are superior to branched-chain hydrocarbons. Cetane, *n*-hexadecane, ignites rapidly and is given a rating of 100, whereas α-methylnaphthalene (Section 8.3) ignites slowly and is rated zero. The *cetane number* of a fuel, then, is the per cent of cetane in a cetane-α-methylnaphthalene mixture which has equal ignition qualities as the sample fuel. Diesel engines have a higher efficiency than gasoline engines and also use less expensive fuel.

Kerosene, C_{12}—C_{15}:

Kerosene is used for domestic heating, illumination, and jet-propulsion fuel. Three hundred gallons of jet fuel are required to taxi a jet bomber from the warm-up ramp to the end of a runway for takeoff, usually a distance of about 1.5 miles.

Gas Oil or Diesel Fuel, C_{15}—C_{18}:

Gas oil is used for fuel in furnaces, diesel engines, and for cracking stock.

Lubricating Oil, C_{16}—C_{20}:

Lubricating oil is used as a lubricant or for cracking stock. It is purified by steam distillation, vacuum distillation, molecular distillation, or extraction. Extraction is made with an alkali to remove acids; treatment with clay is made to remove the last traces of acid; wax is removed by adding propane, chilling, and filtering.

Paraffin Wax, C_{21}—C_{40}:

Paraffin wax is removed chiefly by freezing and filter pressing. It has now become an important basic material in the rapidly expanding packaging industry. The large domestic demand for petroleum wax, about 800 million pounds annually, is due to its very low water permeability. For illustration, the relative water-vapor transmission rates of various packaging materials of approximately the same thicknesses are shown in Table 2.5. We see that waxed paper, with a transmission rate of 0.7, is a superior waterproof and watertight packaging material. The oldest use of wax is in the manufacture of candles, but this use is now small compared to packaging. The milk-carton and frozen-food industries are major consumers of paraffin wax. Even today, the manufacture of candles accounts for more than 75 million pounds of paraffin wax each year. Waxes are also important ingredients in many items such as rubber, polishes, solid lubricants, and paper cups.

TABLE 2.5. RELATIVE WATER-VAPOR TRANSMISSION RATES

Waxed glassine paper	0.7
Cellophane (moisture resistant)	1.0
Saran	1.5
Polyethylene	2.5
Butyl rubber	3.0
Polystyrene	50.0
Cellophane (plain transparent)	500.0
Cellulose acetate	500.0
Unwaxed glassine paper	500.0

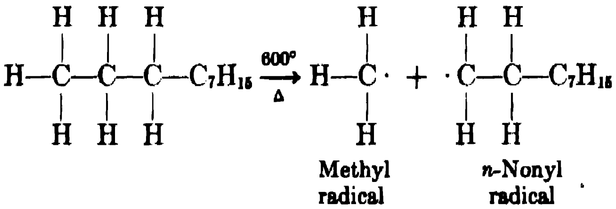
Coke and Asphalt:

Coke and asphalt are used for fuel, underground cables, battery boxes, brake linings, insulation, roofing, paving for playgrounds and roads, and asphalt tiles for flooring.

f. Processes of the petroleum industry.

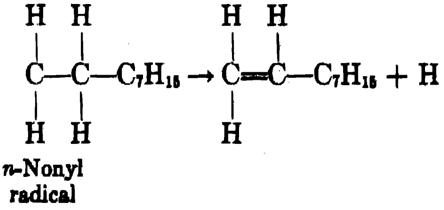
Cracking:

Pyrolysis of hydrocarbons is called *cracking* and consists of the breaking down of hydrocarbons to other hydrocarbons of lower molecular weight. For example, when *n*-decane is heated to a temperature above 600°, the reaction product consists of a mixture of saturated and unsaturated hydrocarbons having from 1 to 10 carbon atoms, and hydrogen gas. The pyrolysis proceeds by a free radical mechanism, and the original carbon chain is broken randomly. For illustration, cleavage at the end of the chain produces the methyl and nonyl radicals:



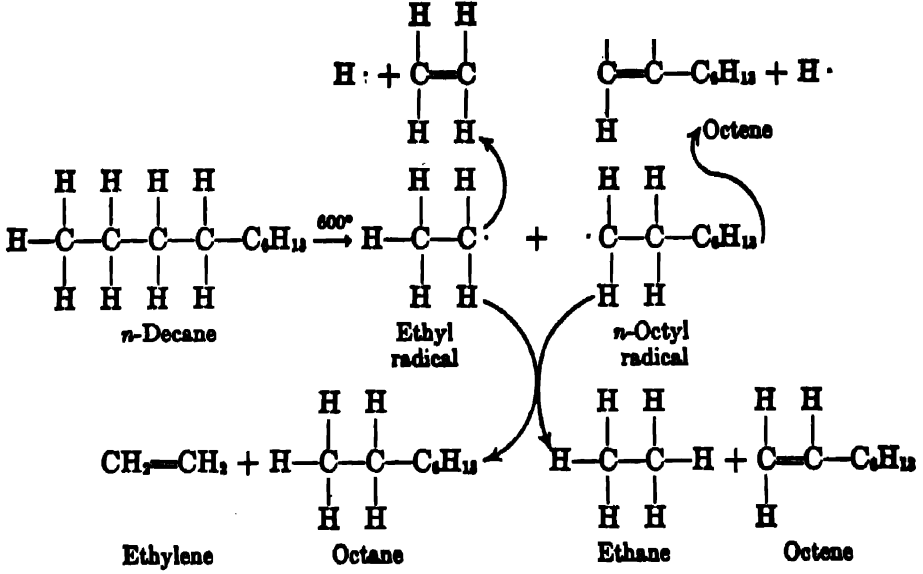
$$H_3C\text{—}CH_2\text{—}CH_2\text{—}C_7H_{15} \xrightarrow[\Delta]{600^\circ} H_3C\cdot + \cdot CH_2\text{—}CH_2\text{—}C_7H_{15}$$

The methyl radical may attack a second decane molecule to produce methane plus a decyl radical (or two methyl radicals may combine to form ethane), and the nonyl and decyl radicals may each lose a hydrogen atom to produce the respective unsaturated hydrocarbons:



$$H_2C\text{—}CH_2\text{—}C_7H_{15} \rightarrow H_2C\text{=}CH\text{—}C_7H_{15} + H$$

The unsaturated hydrocarbons may suffer further cracking, and a hydrogen atom may combine with another hydrogen atom or propagate the chain reaction. Cleavage at the second C—C bond in the decane chain produces ethyl and octyl radicals which may react to produce ethane plus octane or ethylene plus octane.



It can be seen that a great variety of products is produced in the cracking process, and the relative proportions of the different products obtained depend upon the reaction conditions. The unstable free radicals react in at least three ways: (1) by *dimerization*, $R\cdot + R\cdot \rightarrow R:R$; (2) by *disproportionation*, $2RCH_2CH_2\cdot \rightarrow RCH_2CH_3 + RCH{=}CH_2$; and (3) by *radical transfer*, $R\cdot + R'X \rightarrow RX + R'\cdot$. The first two possibilities terminate reaction. In many instances, all occur simultaneously and the mixture of products is very complex. In general, however, certain reactions are favored relative to the others, and specific products predominate.

In the petroleum industry, the raw material for the cracking process is usually gas oil or lubricating oil, and the process accounts for 50 per cent of the total supply of gasoline and practically all the high-octane gasoline. When the process is effected by heat alone, called *thermal cracking*, it is carried out at elevated temperatures and high pressures to give a product of low octane rating. When a catalyst is used, the process is called *catalytic cracking*. This permits the use of lower temperatures and pressures, and the gasoline product has a high octane number. It may be carried out by placing the catalyst on (1) a fixed bed or (2) a moving bed or (3) by adopting a "fluid" catalyst technique whereby the catalyst is powdered and mixed with air to make it flow like a liquid. It is well known that the smaller the particles of a given mass of matter, the greater is their total surface area. The particles of the fluid catalyst are [illegible] that a handful has a surface area equivalent to several acres. Most cracking is now done by the latter method because it is most easily adapted to large-scale runs and is the most efficient. Most cracking catalysts consist of silica and alumina. A large "cat cracker" may produce 1,000,000 gallons of gasoline and 250,000 gallons of fuel oil per day by circulating a boxcar of catalyst per minute. Its regenerator is large enough to contain an eight-room house. Valuable hydrocarbon gases are produced as side products, normally having a composition approximately as given in Table 2.6.

TABLE 2.6. HYDROCARBON GASES PRODUCED BY PYROLYSIS

	Thermal Method (%)	*Catalytic Method* (%)
Hydrogen	4.7	29.6
Methane	32.7	18.0
Ethane	21.6	8.0
Ethylene	2.0	4.0
Propane	17.2	15.0
Propene	7.4	8.0
n-Butane	4.4	3.0
Isobutane	2.0	7.5
Isobutene	3.7	5.2
C_5 plus	2.5	0.0

The gases listed in the table are used extensively for chemical synthesis. Later, when the industrial preparations of alcohols, artificial rubber, acids, etc., are discussed, reference will be made to the cracking process as a source of the starting materials.

Polymerization:

Small hydrocarbon molecules are combined to form larger ones in the gasoline and fuel-oil molecular weight range. (A detailed definition of polymerization is given in Section 3.4.)

Alkylation:

In the petroleum industry this term refers to the combination of unsaturated and saturated hydrocarbons to form fuel oil and *alkylate* gasoline. Sulfuric acid or hydrogen fluoride is often the catalyst.

Hydrogenations:

1. Fischer-Tropsch process

$$CH_4 \xrightarrow{\text{oxidation}} CO \xrightarrow{H_2,\ \text{cat.}} \text{liquid fuel} + \text{oxygenated compounds}$$

This is a German process developed by Fischer and Tropsch to produce low-grade fuels. The Americans have modified the process (with the *Hydrocol*

Synthol processes) to produce 80-octane gasoline at about 7 cents a gallon at the plant. The oxidation products are low-molecular-weight alcohols, aldehydes, ketones, and acids.

2. Bergius process[9]

$$1800^\circ \text{ C.: Coal} + H_2O + O_2 \rightarrow CO \xrightarrow{H_2} \text{liquid fuel (the German process)}$$

$$450^\circ \text{ C.: Coal} + H_2 \rightarrow \text{liquid fuel (American modification)}$$

From one ton of coal, about three gallons of liquid fuel plus oxidation products are obtained. The Germans produced a high-grade fuel by this method. This is not a process of the petroleum industry, but it is so closely related that it can be included here.

3. Destructive hydrogenation. The higher boiling fractions from petroleum, referred to as *heavy crude bottoms*, are first broken down and the fragments are then hydrogenated over catalysts at high pressures to give liquid fuels. This process is not an economic success so far.

Dehydrocyclization:

Known industrially as *hydroforming* or *aromatization*, dehydrocyclization is the conversion of aliphatic hydrocarbons to aromatic hydrocarbons. Hydrocarbons of octane numbers well above 100 are needed in large quantities as additives to gasoline to satisfy present-day high-compression engines. Most aromatic hydrocarbons in the gasoline boiling range have octane numbers above 100. Hydroforming consists of either (1) dehydrogenation of cyclohexanes, (2) isomerization of cyclopentanes to cyclohexanes and dehydrogenation of these, or (3) cyclization of alkanes to cycloalkanes and their subsequent dehydrogenation (cf. Section 8.1). Terms such as *platforming*, *catforming* and *ultraforming* merely refer to variations in conditions and catalysts employed for the process.

Aromatization is used not only to produce aromatic hydrocarbons for high-octane gasoline but also for producing the basic aromatics, benzene, toluene, and xylene. As a result, almost half of all aromatic chemicals are now manufactured from petroleum and natural gas.

Isomerization:

In the petroleum and natural-gas industry, most isomerizations involve the conversion of normal hydrocarbons to branched-chain hydrocarbons.

Dehydrogenation:

Butane and butene are dehydrogenated to butadiene (for production of synthetic rubber), and cyclic hydrocarbons are dehydrogenated to aromatic hydrocarbons.

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[9] F. Bergius, German chemist, shared the Nobel Award in chemistry with C. Bosch in 1931.

Sweetening (or desulfurization):

This is the term for the process by which the remaining sulfur compounds in fuels are removed and by which the foul-smelling sulfur compounds are converted to sweet-smelling ones.

Stabilization:

Stabilization is the adjustment of butane content of gasoline: low in summer to prevent vapor locking of the motor and high in winter to promote easy engine starting.

Sources of gasoline: The four sources of gasoline are petroleum, natural gas, coal, and shale rock.

1. *Petroleum*
    - a. Straight-run—10 per cent of total supply.
    - b. Cracking process—50 per cent of total supply.
    - c. Polymerization and alkylation—10 per cent of total supply.
    - d. Hydrogenation of heavy oils.
2. *Natural gas*
    - a. Extracted by compression or by liquid extraction: called *casing-head gasoline*, it accounts for 10 per cent of total supply.
    - b. By synthesis, such as the Synthol and Hydrocol processes.
3. *Coal*

    By American modifications of the Bergius process.
4. *Shale rock*

Shale rock is a hard, slatelike rock which contains some partly decomposed organic matter called *kerogen*. When shale rock is heated to high temperatures, a viscous, unstable raw oil is liberated in amounts ranging from 5 to 90 gallons of oil per ton of rock. The raw oil contains excessive amounts of sulfur, oxygen, and nitrogen, and it makes a good feed stock for making gasoline, diesel fuel, ammonia, and certain petrochemicals. The deposits of shale rock in the Colorado and Utah area can supply an estimated 300 billion barrels of liquid fuel. Scotland has used shale as a source of fuel on a very low scale for many years. Sweden has a large deposit of shale from which she produces fuel oil, kerosene, and sulfur. Sweden's fishing fleet is largely powered by diesel oil made from shale rock.

g. Petrochemicals industry. Before World War II, the coal-tar, the petroleum, and the natural-gas industries were quite separate from one another, each providing its own line of chemicals. In brief, natural gas supplied gaseous fuel, low-molecular-weight organic chemicals and carbon black; petroleum supplied liquid fuel, aliphatic organic chemicals, and asphalts; coal provided solid fuel, aromatic chemicals, and illuminating gas. Now natural gas and coal can supply liquid fuel in competition with petroleum; petroleum is supplying aromatic hydrocarbons, like benzene and toluene, to supplement the

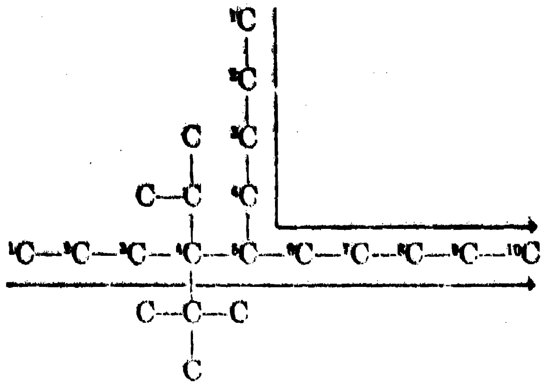
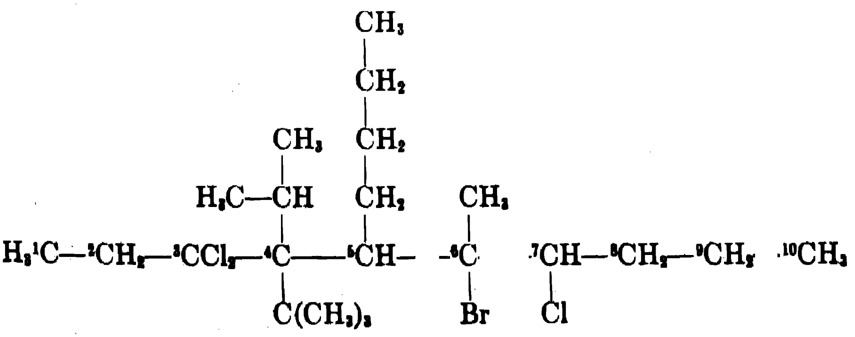


Fig. 1.22. Numbers and arrows to indicate two 10-atom chains in structure I.

chains. In this case, the horizontal chain is chosen, for then the upright branch from C_5 is a simple *n*-butyl group.

After the main chain is selected, the carbon atoms are numbered for reference purposes. One may start at either end of the chain, but it is conventional to start at the end nearest the substituents, for then the prefix numbers which indicate the positions of substituents will be the smaller.

Now, the four initial points of the Geneva system can be followed: (1) The body of the name will be *deca*, based on the fact that there are 10 carbon atoms in the main chain. (2) The suffix is *-ane*, since all the carbon atoms in the main chain form only single bonds. This gives us *decane*, so far. (3) The prefix, indicating the types and positions of substituents, will be more extensive. One goes along the chain from the number 1 carbon atom to the number 10 carbon atom, naming atoms or groups which have been substituted for hydrogen.[11] A carbon atom need not be mentioned unless something has been substituted for hydrogen on that carbon atom. Structure I may be rewritten as Ib, in which the carbon atoms of the main chain have been numbered.



Ib

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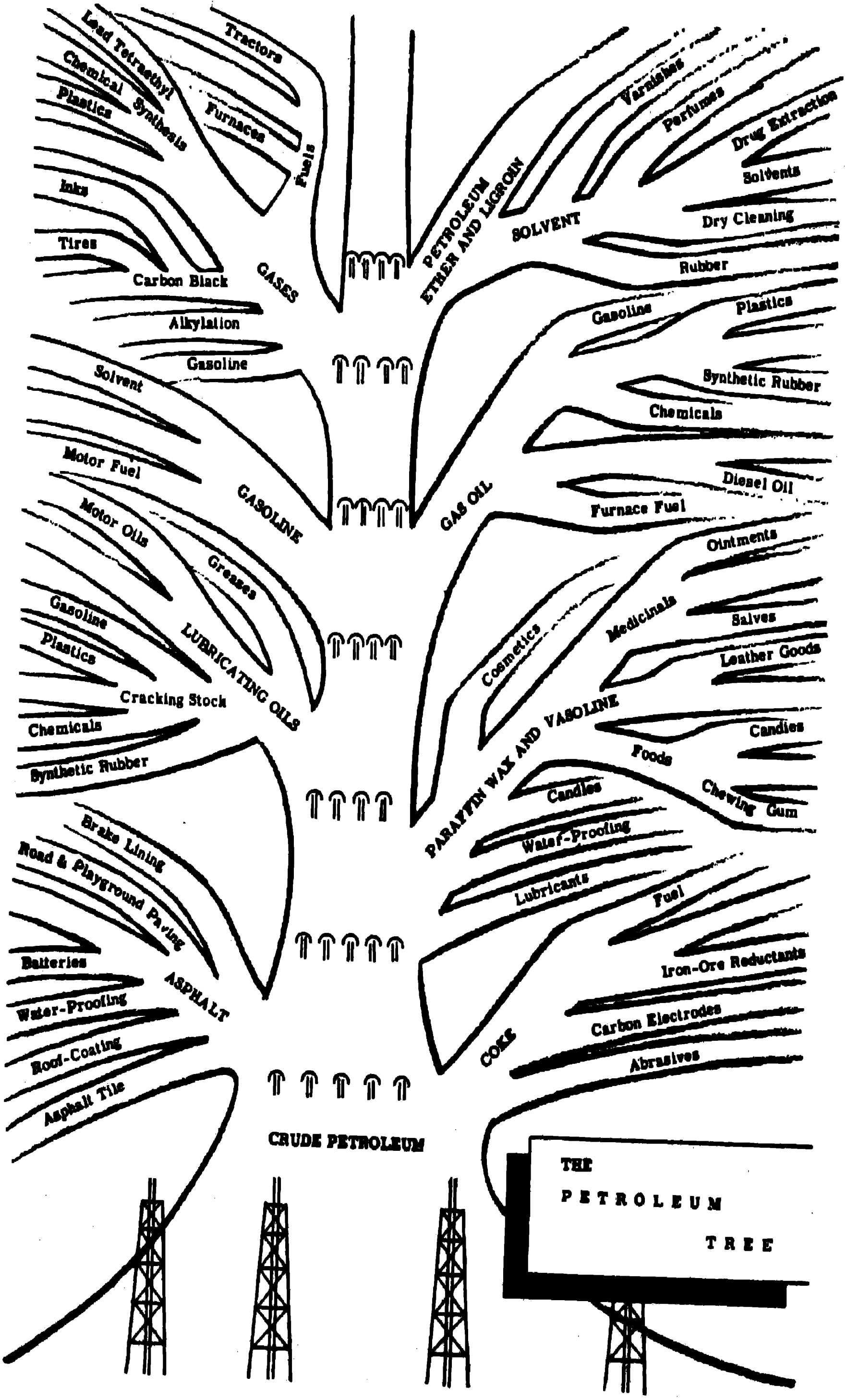
[11] For indexing purposes, the substituents are sometimes listed in alphabetical order irrespective of position.


Lead Tetraethyl
Chemical Synthesis
Plastics
Tractors
Furnaces
Fuels
Inks
Tires
Carbon Black
GASES
Alkylation
Gasoline
Solvent
Motor Fuel
GASOLINE
Motor Oils
Greases
Gasoline
Plastics
LUBRICATING OILS
Cracking Stock
Chemicals
Synthetic Rubber
Brake Lining
Road & Playground Paving
Batteries
ASPHALT
Water-Proofing
Roof-Coating
Asphalt Tile
PETROLEUM ETHER AND LIGROIN
Varnishes
Perfumes
Drug Extraction
Solvents
SOLVENT
Dry Cleaning
Rubber
Gasoline
Plastics
Synthetic Rubber
Chemicals
Diesel Oil
Furnace Fuel
GAS OIL
Ointments
Cosmetics
Medicinals
Salves
Leather Goods
PARAFFIN WAX AND VASOLINE
Candies
Foods
Chewing Gum
Candles
Water-Proofing
Lubricants
Fuel
Iron-Ore Reductants
Carbon Electrodes
COKE
Abrasives
CRUDE PETROLEUM
THE PETROLEUM TREE

10. Give the names and formulas of the chief components of the following: marsh gas, petroleum ether, ligroin, natural gas, and kerosene.

11. In a sentence or by an equation, cite a contribution made to organic chemistry by the following persons: G. N. Lewis, V. Grignard, Wurtz, Bergius, and Paneth.

12. The refractive indexes at 20° of *n*-hexane, *n*-heptane, and *n*-octane are approximately 1.37, 1.38, and 1.39, respectively. What would you expect the index of refraction of *n*-decane to be, and what principle do you use in making such an estimation?

13. Write equations for the preparation of *n*-butane from (a) *n*-butyl chloride, (b) ethyl bromide, (c) 1-butene, (d) $CH_3CH_2CO_2Na$, (e) *sec*-butyl bromide.

14. Give the structural formulas for the products of the following reactions, and list the products in order of increasing boiling points:

(a) *t*-butyl bromide plus sodium metal,
(b) electrolysis of $(CH_3)_2CH—CH_2—CO_2K$,
(c) *n*-octyl bromide plus magnesium, then water.

15. Under which set of conditions would you expect the higher proportion of monobromination products:

(a) slow addition of 160 g of bromine to 100 g of *n*-pentane;
(b) slow addition of 100 g of *n*-pentane to 160 g of bromine.

TEST QUESTIONS, Set 2

1. Describe in detail the procedure and apparatus you would use to remove impurities of hydrogen chloride and water vapor from a sample of methane gas.

2. Can homologs be isomers? Why, or why not?

3. Show by equations how the following paraffins could be synthesized: (a) 2,2-dimethylheptane, (b) 3,4-dimethylhexane, (c) 2,2,5,5-tetramethylhexane.

4. Prepare *n*-decane from an organic carboxylic acid.

5. Write the structural formulas and names of the isomeric heptanes.

6. Show by equations the series of reactions by which ethane could be converted into *n*-butane industrially.

7. Which of the following formulas might designate members of the paraffin series: C_2H_7, C_5H_{12}, C_3H_6, C_4H_9, $C_{10}H_{22}$, $C_{11}H_{22}$? Change the subscripts for H so that all represent paraffins.

8. If 10 g of propane were burned in contact with 30 liters of gaseous oxygen, both STP, how much propane or oxygen would remain unreacted? What weight of water would be produced?

9. What volume of 2,3-dimethylbutane, measured at 136.5° and 0.8 atmospheric pressure could be prepared from 12.3 g of the proper alkyl bromide by the Wurtz reaction?

10. What would be the normality of hydrobromic acid if the HBr from the bromination of isopentane with 80 g of liquid bromine were collected in 225 ml of water?

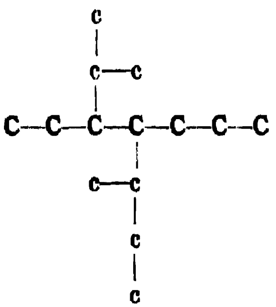
11. Which alkane has a molecular weight of 86 and will form (a) two monobromo derivatives, (b) three monobromo derivatives, (c) four monobromo derivatives? How many dibromo derivatives will each form?

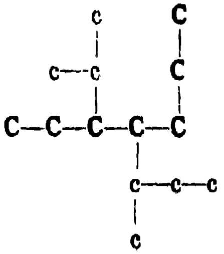
12. The densities of some normal alkanes are as follows:

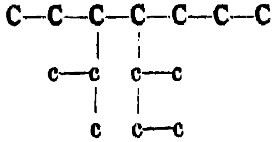
pentane	0.626
hexane	0.659
heptane	0.684
nonane	0.718
undecane ($C_{11}H_{24}$)	0.740

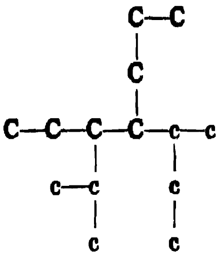
out straight, but in Ic it was bent upward. Notice that if the ^{5}C—^{6}C carbon-carbon bond in Id were to rotate 120°, it would swing the ^{7}C—^{10}C carbon chain upward and bring the ^{6}C—^{7}C branch level with the ^{1}C—^{6}C chain, as the molecule appears in Ic. Because of the ease of rotation, this may happen so that two samples of the material cannot be obtained in which all the molecules in one sample would have configuration Ic and all molecules in the other sample would have configuration Id. The ease at which one configuration passes into the other prevents the isolation of a sample in which all molecules have only one configuration. Actually, molecules do not assume all possible configurations but only those that are the most stable.

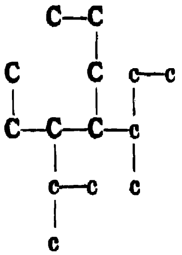
Because of such rotation, one must get accustomed to seeing the same group twisted in one of several possible configurations. For example, the following configurations may be given for 3-isopropyl-4-*sec*-butylheptane, and they differ merely by rotations about various C—C bonds. To avoid confusion, only the carbon skeletons are shown, and the same seven-atom chain is in bold face in each structure for the student's orientation.





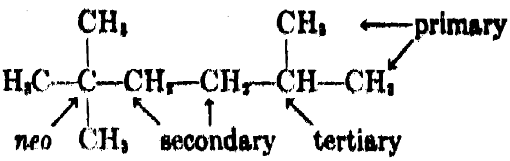




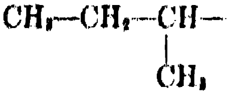
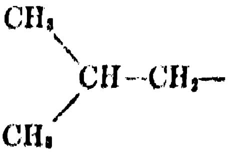
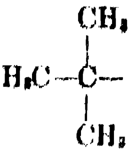


Many others could be given. The point to be emphasized is that organic molecules, in the liquid or gaseous states or in solution, are twisting about like this continuously. This is particularly true for long-chain molecules.

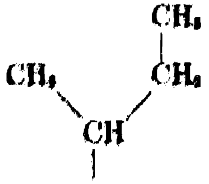
One additional point about nomenclature can be mentioned. In a strict sense, any organic compound can be considered as a derivative of methane where various groups have been substituted for one or more of the methane hydrogens. Thus, $(CH_3)_2CH—CH_2—CH_3$ may be called dimethylethylmethane, or isopropylmethylmethane, or isobutylmethane, where first the third from right, then the second from right, then the right-end carbon atom is



The butyl groups may now be discussed; they are as follows:

$CH_3—CH_2—CH_2—CH_2—$	*n*-Butyl group
 $CH_3—CH_2—\underset{CH_3}{\underset{\mid}{CH}}—$	Secondary-butyl group (*sec.*-butyl or *s*-butyl)
	Isobutyl group (*i*-butyl)
 $H_3C—\underset{CH_3}{\underset{\mid}{\overset{CH_3}{\overset{\mid}{C}}}}—$	Tertiary-butyl group (*tert.*-butyl or *t*-butyl)

It can be observed that there are two types of carbon skeletons here. For the straight chain of carbon atoms, there are two different butyl groups. The name *sec*-butyl is used to indicate that the straight chain is to be attached by one of the secondary carbon atoms, either one giving rise to the same butyl group. Thus, the two secondary carbon atoms in *n*-butane are equivalent and a hydrogen atom removed from either one produces the same *sec*-butyl group; *i.e.*, $CH_3—\overset{\mid}{CH}—CH_2—CH_3$ is identical to $CH_3—CH_2—\overset{\mid}{CH}—CH_3$, but the two are oriented differently in space. The two models can be turned around in space to occupy identical volumes, or in different words, they would fit the same mold. This is referred to as being *spatially identical.* At the same time, because of free rotation, the *sec*-butyl group may have another conformation such as



where the ethyl group has rotated about the center C—C bond. The ball-and-stick models of the corresponding *n*-butane molecules are shown in Figure 1.21.

The scheme of naming a secondary hydrocarbon group can only be used atom is quadricovalent instead of bicovalent and that the four bonds are equivalent. It is also possible for the 2*s* and two of the 2*p* orbitals of carbon to merge to form three sp^2 hybrid orbitals, as described for boron in Section 1.1. This still leaves a 2*p* orbital about carbon, containing an unpaired electron. This approximates the situation for carbon in carbon-carbon double bonds. Since three sp^2 orbitals are coplanar and form 120° bond angles, the three atoms attached to such a carbon atom lie in the same plane as the carbon atom. In ethylene, each carbon atom is coplanar with the attached hydrogen atoms and also coplanar with each other; hence, all six atoms lie in the same plane. At each carbon atom there is a *p* atomic orbital perpendicular to the plane of the molecule and containing an unpaired electron, indicated by the propeller-shaped loop (Figure 3.1). A more stable system results by

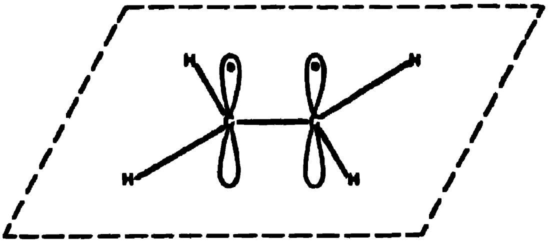
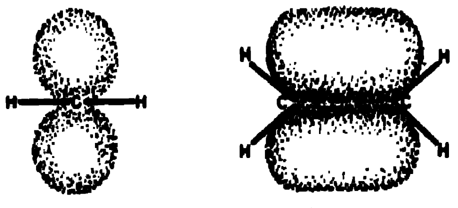


Fig. 3.1.

the two *p* atomic orbitals coalescing to form a molecular orbital which encompasses both carbon nuclei. The resulting molecular orbital resembles two sausages above and below the plane of the molecule (Figure 3.2). Such an orbital is called a *pi* (π) *orbital*, the electrons involved are called *pi electrons*, and the bond is a *pi bond.*



End view Side view

Fig. 3.2. Shape of the pi orbitals in ethylene.

The *p* atomic orbitals at two adjacent atoms will overlap most when they are parallel to each other, but since the overlap is less than that of the sp^2—sp^2 orbitals for the first C—C bond (called a *sigma* (σ) *bond*), the π bond is not as strong as the sigma bond. For instance, the energy of the σ C—C bond is about 80 kcal, whereas that of the π bond is about 65 kcal. The π electrons are held less firmly than σ electrons and can more easily be polarized (that is, attracted to either end of the molecular orbital by an external charge) than σ electrons, so the π electrons are commonly referred to as *mobile electrons*, whereas the σ electrons are said to be *localized.*

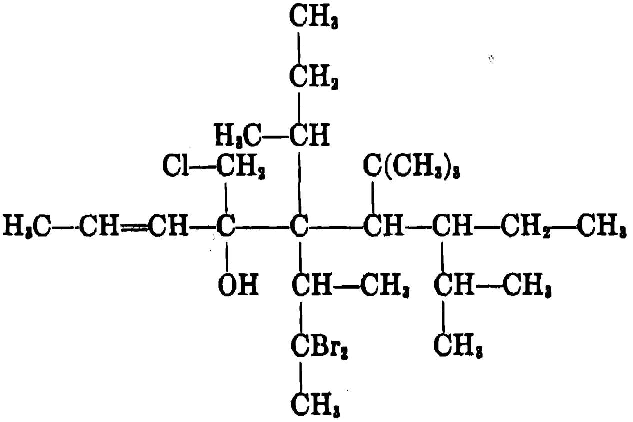
3.1 NOMENCLATURE

The only new aspect of the Geneva system to be learned for naming alkenes concerns the suffix for indicating the class of compound. The position of the functional group is indicated by a number which may either precede or follow the name. In this country, the common practice is to have the number just precede the body of the name. The class ending for the alkenes is *-ene*. For example, a four-carbon chain with the double bond after the first carbon atom is called 1-butene, C═C—C—C, and a six-carbon chain with the double bond after the third carbon is called 3-hexene, C—C—C═C—C—C. The numbering of carbon atoms normally starts at the end nearest the double bond.

The other three basic points of nomenclature concerning the number of carbon atoms in the main chain, and the naming of substituents and branch chains, are the same as was illustrated for alkanes. For practice, the structure of the compound 4-hydroxy-4-chloromethyl-5-*sec*-butyl-5-(α-methyl-β,β-dibromopropyl)-6-*t*-butyl-7-isopropyl-2-nonene is worked out below.

Steps 1 and 2: From the portion 2-nonene, write down nine carbons in a row with a double bond following the second: C—C═C—C—C—C—C—C—C.

Steps 3 and 4: Now, the substituents are attached to the respective carbons. Observe that point 4 is invoked to take care of the substituted branch at C_5. After the covalence of each carbon is brought to 4 by attaching the required number of hydrogen atoms, the resulting structural formula is



As has been stated before, the first few members of the various classes of compounds frequently have trivial names which are more common than the I.U.C. names. So it is with alkenes; the first three[1] have common names as given in Table 3.1.

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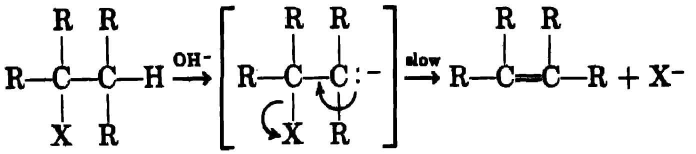
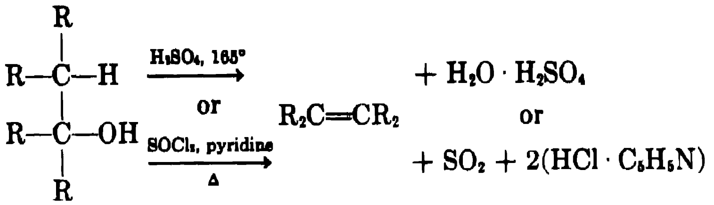
[1] The pentenes were formerly called *amylenes*, but the present trend is to employ the I.U.C. name to avoid ambiguity.



$$R-\overset{R}{\underset{X}{C}}-\overset{R}{\underset{R}{C}}-H \xrightarrow{OH^-} \left[R-\overset{R}{\underset{X}{C}}-\overset{R}{\underset{R}{C}}:^-\right] \xrightarrow{slow} R-\overset{R}{C}=\overset{R}{C}-R + X^- \qquad (b)$$

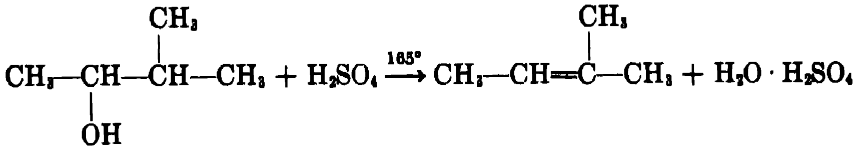
Simple alkyl halides react via the concerted mechanism (a), although certain cyclic compounds undergo dehydrohalogenation by the stepwise mechanism (b).

2. Dehydration of alcohols



$$R-\overset{R}{C}-H \atop R-\underset{R}{C}-OH \quad \begin{matrix} \xrightarrow{H_2SO_4,\ 165^\circ} \\ \text{or} \\ \xrightarrow[\Delta]{SOCl_2,\ pyridine} \end{matrix} \quad R_2C=CR_2 \quad \begin{matrix} + H_2O\cdot H_2SO_4 \\ \text{or} \\ + SO_2 + 2(HCl\cdot C_5H_5N) \end{matrix}$$

In each of these general equations the R's may be alkyl groups or hydrogen atoms. The symbol R is used to make the equations very general. For illustration of a specific example, a preparation of 2-methyl-2-butene would be as follows:



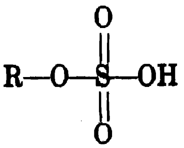
$$CH_3-\underset{OH}{CH}-\overset{CH_3}{CH}-CH_3 + H_2SO_4 \xrightarrow{165^\circ} CH_3-CH=\overset{CH_3}{C}-CH_3 + H_2O\cdot H_2SO_4$$

As in the dehydrohalogenation, the H and OH may be split out in two different directions with the formation of two products, $CH_2=CH-CH(CH_3)_2$ and $CH_3-CH=C(CH_3)_2$, but the major product is in accordance with Saytzeff's rule.

In dehydration with sulfuric acid, an intermediate alkyl hydrogen sulfate may be formed which can be isolated if desired.

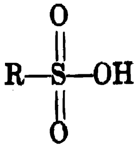
$$R_2CH-CR_2OH + HOSO_3H \rightarrow \underset{\substack{\text{An alkyl}\\ \text{hydrogen sulfate}}}{R_2CH-CR_2OSO_3H} + HOH$$

Observe that in an alkyl hydrogen sulfate, there is a C—O—S bond, whereas in an alkylsulfonic acid there is a C—S bond.



$$R-O-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-OH$$

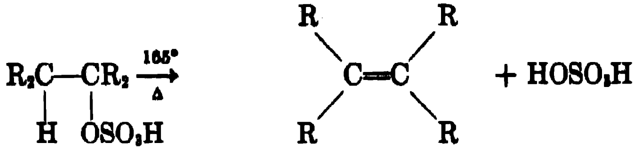
Alkyl hydrogen sulfate



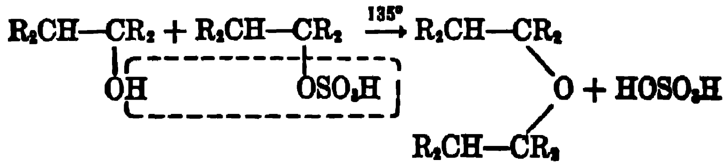
$$R-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-OH$$

Alkylsulfonic acid

Alkyl hydrogen sulfates are syrupy liquids like sulfuric acid. When they are heated to temperatures above 150°, they decompose with the loss of $HOSO_3H$ to produce an alkene.



Normally the alkyl hydrogen sulfate is not isolated, and during its formation from the alcohol, some of it will react with the alcohol to produce an ether. Instead of the OSO_3H portion of the alkyl hydrogen sulfate stripping an H atom from within the molecule, as it does when forming the alkene, it will take the H atom from the OH group of an alcohol molecule, and at a lower temperature:



or, with simpler formulas, $R{-}OSO_3H + R'OH \rightarrow R{-}O{-}R' + HOSO_3H$. Therefore, some ether and some alkene are obtained in the reaction. If the ether is desired, the reaction is run at a lower temperature and with the use of excess alcohol; if the alkene is desired, the reaction is carried out at the higher temperature. In either case, the main product is contaminated with the other product and the impurity must be removed by some method of purification.

It can already be seen that organic reactions are complex, with many side products being formed. The dehydration of alcohols is a good example of how the course of an organic reaction can be directed by controlling the conditions. If ethyl alcohol is allowed to react with an excess of sulfuric acid at moderate temperatures, ethyl hydrogen sulfate is formed:

$$C_2H_5OH + HOSO_3H \xrightarrow{\text{room temp.}} C_2H_5OSO_3H + HOH$$

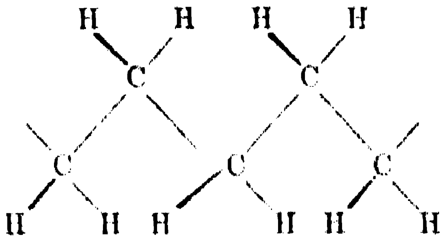
If the ethyl hydrogen sulfate is heated in the presence of more alcohol to slightly higher temperatures, ethyl ether is produced:

$$C_2H_5OSO_3H + C_2H_5OH \xrightarrow[\Delta]{135°} (C_2H_5)_2O + HOSO_3H$$

If the $C_2H_5OH{-}H_2SO_4$ reaction mixture is heated to the point where ethyl hydrogen sulfate decomposes, about 165°, ethylene is formed:

$$C_2H_5OSO_3H \xrightarrow[\Delta]{165°} CH_2{=}CH_2 + HOSO_3H$$

The side view of *n*-butane reveals the Z-shaped configuration of the carbon chain in the *trans* conformer, and it can be understood why a saturated hydrocarbon carbon chain has a zig-zag shape.



In this conformation, each CH_2 group is *trans* across the C—C bond to give the least amount of repulsion between neighboring groups.

STUDY EXERCISES

1. Write the structural formulas for (a) the first ten normal alkanes; and (b) the methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, *tert*-butyl, *sec*-butyl, and the *n*-decyl groups.

2. Write graphic formulas for the following compounds:

(a) 2-methyl-3-ethylhexane
(b) 3,3,4-trimethylheptane
(c) 4-isopropyl-6-methylnonane
(d) 3-*tert*-butyl-4-*sec*-butyl-5-*n*-butyl-6-chloromethyldecane.

3. Name the following compounds:

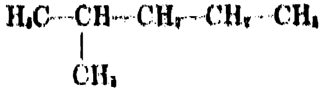
(a) $(CH_3)_2CH—CH(C_2H_5)—CH_2—CH_2—CH_2—CH_3$
(b) $CH_3—CH_2—C(CH_3)_2—CH(CH_3)—CH_2—CH_2—CH_3$
(c) $CH_3—CH_2—CH_2—CH(CH_2Cl)—CH_2—CH_3$

4. Give an example of chain, position, functional, geometric, and optical isomers.

5. Pick out the primary, secondary and tertiary carbons in the molecules of Problem 2.

TEST QUESTIONS, Set 1

1. Give three names for the compound



$$H_3C—\underset{\displaystyle CH_3}{\underset{|}{CH}}—CH_2—CH_2—CH_3$$

2. Give the graphic formulas and names for the isomers having the molecular formula $C_5H_{11}Br$ (8 possible).

3. Give the structural formulas and names for the isomers having the molecular formula $C_5H_{10}Br_2$ (21 possible).

4. What are the structural formulas for neopentane and the neopentyl group?

5. Which formulas in the following list represent identical molecules:

regarded as the methane carbon atom. This scheme can be used for simple molecules without any difficulty, although sometimes it is illogical. It is often absurd for complex molecules.

When a compound is named as a derivative of an actual substance, the name is written as one word, with hyphens used to separate numbers or just for clarity. Thus, propane is a definite compound, and names of its derivatives are written as one word, as for example, 1-chloropropane or 2-hydroxypropane. On the other hand, chloride and alcohol are not the names of actual compounds but of two classes of compounds. Hence, *n*-propyl chloride or isopropyl alcohol (for the two compounds just mentioned) are each written as two words.

This section has covered the basic points of the Geneva system. There are several additional rules to be learned which take care of the various classes of open-chain and cyclic structures. These rules will be incorporated into the system as new classes of compounds are encountered.

It is noteworthy that the Geneva system is continually being revised in order to take care of new, complex organic molecules. In recent years chemists have been trying to develop systems for the codification of organic substances. Particularly for card indexing, a system of linear notation is sought which would provide a unique code name or line formula for each compound and which would reveal as much information as possible about the compound. Several systems have been devised, and for examples, the code names of two compounds by four of these systems are as follows:

Common Name	*Dyson*	*Gruber*	*Silk*	*Wiswesser*
Isopropyl alcohol	C_3.Q,2	C3.20H	CQC	QY
Benzoic acid	B6.CX	(6)CX	B.X	QVR

These systems are receiving critical evaluation by international committees with respect to speed of coding and decoding names, simplicity, ability to handle all types of structures, and other pertinent points.

1.6 ISOMERISM

As defined in Section 1.1, isomers (Gr., *isos*, the same, and *meros*, parts) are substances having the same molecular formula but different molecular structures. Isomerization is the process of going from one isomer to another, and isomerism is the phenomenon that isomers exist. Several forms of isomerism are possible and these are outlined in Table 1.8.[13]

TABLE 1.8. OUTLINE OF TYPES OF ISOMERS

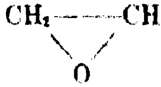
A. Structural Isomers	*B. Stereoisomers*
1. Chain	1. Geometric
2. Position	2. Optical
3. Functional	

---

[13] It will be seen later that certain types of isomers which still fall under this general classification are denoted by special names such as tautomers, epimers, anomers, and conformers.

cannot be collected in separate vessels because of the "spontaneous" transformation of either form into the other by easy rotation about the C—C single bond.

Some 1,2-disubstituted ethanes have trivial names based on a system of nomenclature used before the adoption of the Geneva system. Thus, 1,2-dichloroethane is called *ethylene chloride*. The name may be confusing because the compound does not possess a $C{=}C$ bond as suggested by the name ending, *-ene*. On the other hand, 1,2-dichloroethylene, $HClC{=}CHCl$, does have a $C{=}C$ bond. The names of the two types of compounds differ in the fact that substituted ethylenes ($C{=}C$ compounds) have the names of the substituents preceding and attached to the word *ethylene* while 1,2-disubstituted ethanes have names of substituents to follow the word *ethylene*. Several other common 1,2-disubstituted ethanes are

Ethylene bromide	$Br—CH_2CH_2—Br$
Ethylene glycol	$HO—CH_2CH_2—OH$
Ethylene chlorohydrin	$Cl—CH_2CH_2—OH$
Ethylene cyanohydrin	$HO—CH_2CH_2—CN$
Ethylene oxide	

The second form of stereoisomerism arises when there is no plane of symmetry in a molecule. For example, the tetrahedral model of fluorochlorobromomethane would look like Figure 1.25 (some attention being given to relative sizes of atoms). Observe that an imaginary plane, about which one side would be a mirror image of the other side, cannot be passed through the molecule, whereas this is possible for fluorochloromethane (Figure 1.26).

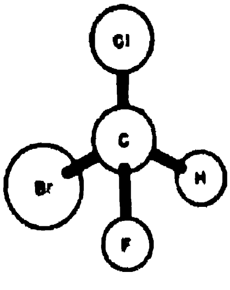


Fig. 1.25.

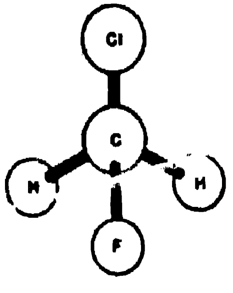
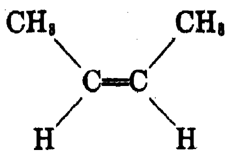
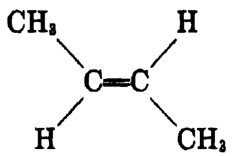


Fig. 1.26. Plane of symmetry passes through the Cl—C—F axis.

The most common organic molecules lacking a plane of symmetry are those in which at least 1 carbon atom has 4 different atoms or groups attached to it. Whenever this is the case, there will be two alternative arrangements of the groups about the carbon atom, such that the two resulting molecules are mirror images of each other. That is, when either molecule is placed before a mirror, its reflection is identical to the other isomer (Figure 1.27).





	cis-2-Butene	*trans*-2-Butene
Boiling point	+3.73°	+0.3°
Melting point.	−139.3°	−105.8°

Similarly, geometric isomers may have spectra (cf. Figure 3.3) that resemble each other over most of the range but are different in certain regions. Usually, *cis* isomers are characterized by an infrared band in the 680–725 cm^{-1} range and *trans* isomers have a band in the 960–990 cm^{-1} region.

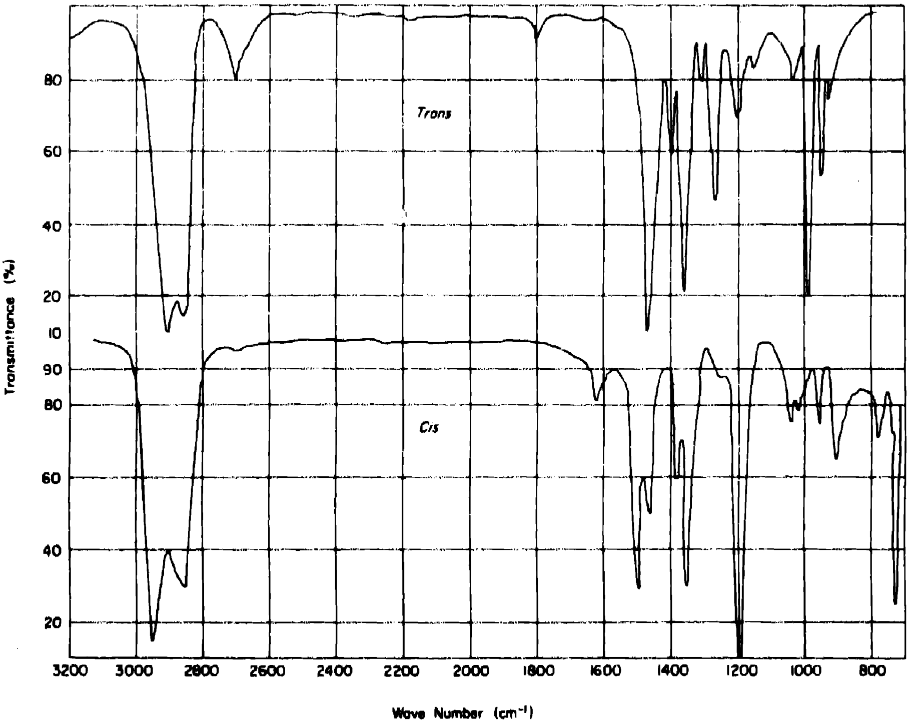


Fig. 3.3. Infrared spectra of *cis*- and *trans*-1,2-di-*t*-butylethylene.

Always one isomer is more stable than the other, although the difference may be small, and normally a sample of an alkene will consist of a mixture of the two with one in predominance. This is of little concern for most purposes, but occasionally the pure isomers will be desired and are obtained by fractionation or a selective synthesis.

3.4 CHEMICAL PROPERTIES

There are four common broad types of reactions in organic chemistry from which standpoint the alkanes and alkenes may be compared:

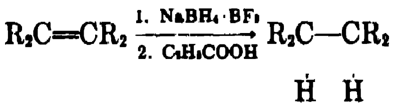
Type of Reaction	*Alkane*	*Alkene*
Reduction	Does not occur	Readily by catalytic hydrogenation
Oxidation	Extremely difficult	Very easy
Substitution	Main type of reaction	Negligible
Addition	Does not occur	Occurs readily

The chemical properties of alkenes will now be discussed on the basis of these four types of reactions:

1. *Reduction.* It is frequently convenient to associate the relative state of oxidation of a compound with the quantity of combined oxygen or the state of reduction with the quantity of combined hydrogen. The H/C ratio in methane is the highest; hence, carbon is regarded as being at its highest state of reduction or lowest state of oxidation in methane. In any other alkane, C_nH_{2n+2}, the H/C ratio is the highest for the corresponding number of carbon atoms, and therefore, the average state of reduction of all the carbons in the compound is the highest. No further reduction can occur unless the compound undergoes fission. In an alkene whose empirical formula is C_nH_{2n}, however, the H/C ratio is lower than in an alkane and one can expect the alkene to be reducible with hydrogen in the presence of a catalyst. Essentially, all reactions involving hydrogen require a catalyst, and three common catalysts are platinum, palladium, and nickel. The general equation for the hydrogenation of an alkene may be written

$$C_nH_{2n} + H_2 \xrightarrow{\text{Ni}} C_nH_{2n+2}$$

On the other hand, this reaction may be conveniently carried out in the laboratory by the use of sodium borohydride:



$$R_2C{=}CR_2 \xrightarrow[\text{2. } C_2H_5COOH]{\text{1. } NaBH_4\cdot BF_3} \underset{H}{R_2C}{-}\underset{H}{CR_2}$$

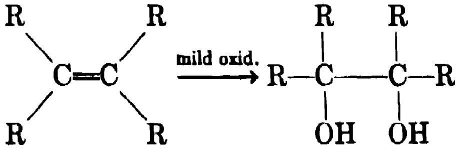
Good yields are obtained and no special apparatus is required.

2. *Oxidation.* It was stated in Section 2.7 that alkanes are inert toward the strong oxidizing agent, potassium permanganate. For practical purposes, then, they are not oxidized chemically. In contrast to this, alkenes are oxidized very easily. A very dilute aqueous solution of $KMnO_4$ is quickly reduced, wherein the pink solution is decolorized or a brown precipitate is formed, depending upon the *p*H. This reaction, known as ***Baeyer's test for unsaturation***, is used to distinguish saturated from unsaturated hydrocarbons in the absence of other easily oxidizable substances.

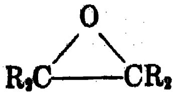
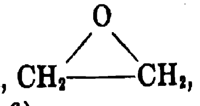
The oxidation or reduction of an organic compound requires one important consideration that is not given to ionic substances. When the oxidation or reduction of an inorganic substance is planned, one merely chooses a reagent that has the required potential. But, in the oxidation or reduction of organic substances, the mechanism of reaction is a major factor in determining whether or not a given reagent may be used. For example, Zn + $HCl_{conc.}$ will reduce ketones ($R_2C{=}O$) all the way down to the corresponding hydrocarbons (R_2CH_2), but $LiAlH_4$ only reduces a ketone to the alcohol (R_2CHOH) which is a higher oxidation state than a hydrocarbon, as shown by the presence of oxygen. This comparison would suggest that Zn + HCl is the stronger reducing agent. On the other hand, $LiAlH_4$ will reduce carboxylic acids (RCOOH) to the corresponding alcohols (RCH_2OH), whereas Zn + HCl will not reduce the carboxylic acids, which implies the opposite relative reducing powers of these two reagents.

Consequently there are specific oxidizing and reducing agents to be used for most redox reactions in organic chemistry. There is no general rule for predicting which reagents may be used, and only by experiment have organic chemists learned these reagents. For most oxidations or reductions of the various classes of compounds, the student will be told one or two reagents that may be used and these will have to be remembered.

During most oxidations of organic compounds, either a C—C or a C—H bond is broken, and the bond to carbon is replaced by an OH group. For example, when an alkene is oxidized under certain conditions, the first change to occur is the cleavage of one of the bonds of the olefin group with replacement by OH groups on the two carbon atoms.



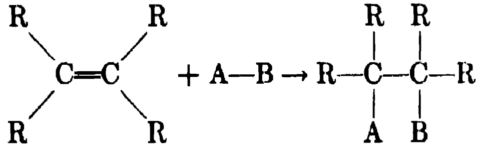
Alkene 1,2-Glycol

Two agents that will do this generally are hydrogen peroxide in glacial acetic acid (pure acetic acid) and dilute potassium permanganate in aqueous sodium carbonate. The oxidizing power of potassium permanganate is greatly reduced in near-neutral solutions; hence, the reaction is performed in aqueous sodium carbonate to maintain a mildly basic medium. A glycol is a compound containing two OH groups, and when the two OH groups are on adjacent carbon atoms, the compound is a 1,2-glycol. As a single statement then, it can be said that *the mild oxidation of an alkene with either hydrogen peroxide in glacial acetic acid or with potassium permanganate in aqueous sodium carbonate yields a 1,2-glycol.* In fact, this mild oxidation of alkenes is one general method of preparing 1,2-glycols. Under controlled conditions, the intermediate epoxy compound, , can be isolated. The most important of such compounds is ethylene oxide, , which is discussed with the aliphatic ethers (see Section 11.6).

Oxidation of alkenes with other oxidizing agents yields a variety of products, depending upon what reagent is used (page 487). The oxidation products include aldehydes, ketones, and carboxylic acids; this is discussed in Section 10.7.

3. *Substitution.* A substitution reaction is one in which some new atom or group replaces an atom or group already a part of a molecule. Practically all chemical reactions of the alkanes, except dehydrogenation, are substitution reactions where one or more hydrogen atoms are replaced, e.g., R—H + X—X → R—X + HX.

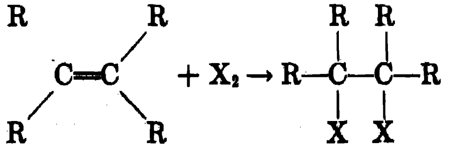
4. *Addition.* An addition reaction is one in which two molecules react to yield a single product. There is a complete union of the two molecules. Alkenes do this easily because many reactants will add to the two carbon atoms joined by the double bond.



Addition reactions are much faster than substitution reactions; alkenes, therefore, undergo addition reactions rather than substitution reactions.

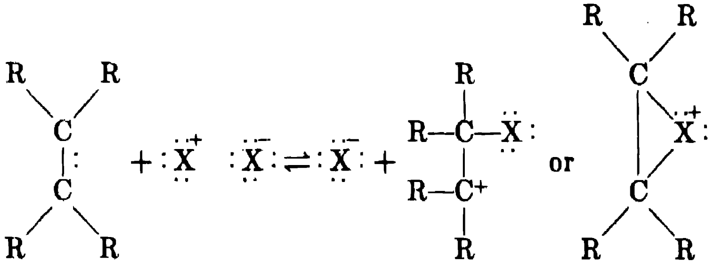
All compounds containing multiple bonds readily undergo addition reactions. One way of explaining the greater reactivity of multiple bonds is to say that an atom forming a multiple bond has not used up all its combining power, and because of its tendency to use all its valence, it readily breaks the multiple bond to form all single bonds. Another way of accounting for the reactivity of multiple bonds will be given in Section 5.3 in terms of "bond strain." A more modern explanation is based on the mechanism of reactions, as illustrated below for the addition of halogens, in which, because of the basicity of the alkene, it forms an intermediate with electron-pair acceptors, and the intermediate undergoes a change to yield the addition product.

a. Halogens. A very common addition reaction of alkenes is their addition of halogens.

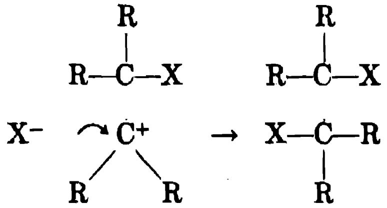


In practice, the reaction is limited to Cl_2 and Br_2, since fluorine reacts too violently for control and iodine does not generally yield stable 1,2-diiodo derivatives. 1,2-Diiodo compounds usually decompose into iodine and an olefin. For example, 1,2-diiodoethane slowly dissociates into ethylene and iodine upon standing in the open. The reaction is reversible, the equilibrium constant having a value of 28 at 30° and 129 at 50° C.

The most simple picture of this reaction would be the simultaneous addition of the two halogen atoms from a single halogen molecule to add onto the adjacent olefinic carbon atoms. From several experimental facts it appears that this is not the mechanism of the reaction. Instead, a stepwise reaction occurs with a polarized halogen molecule to produce a positively charged intermediate.



The structure of the organic intermediate is not known conclusively. Next, a halide anion reacts with this complex, approaching from the rear to yield the addition product (see Section 5.4):

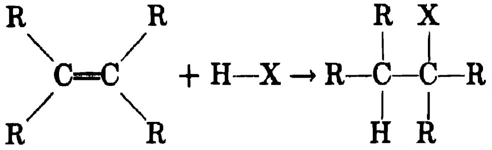


It is known that the halogen must be polarized (or dissociated), because pure ethylene in a waxed container, i.e., nonpolar environment, does not add bromine. Thus, the walls of ordinary glassware or catalytic impurities polarize halogen molecules to initiate reaction. Moreover, the halide ion reacting in the second step is not the same one released in the first step, because when bromine is reacted with an alkene in a solution containing anions, some of the addition product will be found to contain the anion. For example, bromination of ethylene in aqueous sodium chloride yields bromochloroethane plus dibromoethane.

At high temperatures substitution rather than addition may occur. This is due to the formation of halogen atoms, which are highly reactive. Reaction takes place by a free radical mechanism instead of a polar mechanism.

Halogenation is a simple reaction to perform and provides another method for a qualitative test for unsaturation. Saturated hydrocarbons react with halogens, but very slowly in the absence of a catalyst. Furthermore, when alkanes do react, they do so by substitution, which liberates HX. Consequently, if a sample rapidly decolorizes a dilute solution of bromine, it must be unsaturated; as a check, it must do so without the evolution of HBr. A slow reaction with the evolution of HBr is an indication of a saturated hydrocarbon, or at least of a substitution reaction. The reaction may also be used to determine the amount of an olefin in a mixture of hydrocarbons by titrating the mixture with a standardized solution of halogen. For example, this technique is used for fat analyses (cf. Section A-4).

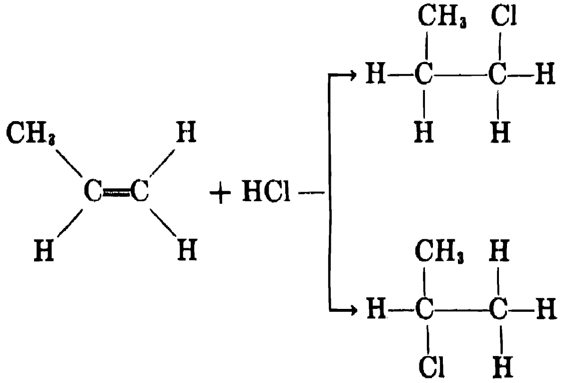
b. Polar compounds. Many polar molecules readily add to alkenes. For hydrogen halides, the equation is as follows:



$R_2C{=}CR_2 + H{-}X \rightarrow R_2CH{-}CXR_2$

HI > HBr > HCl

It is immediately apparent that when the two olefinic carbon atoms are not identically substituted, then there is a possibility for two products to result. An example is the addition of HCl to propene:



$CH_3CH{=}CH_2 + HCl \rightarrow CH_3CH_2CH_2Cl$ or $CH_3CHClCH_3$

1-Chloropropane
or
n-Propyl chloride

2-Chloropropane
or
Isopropyl chloride

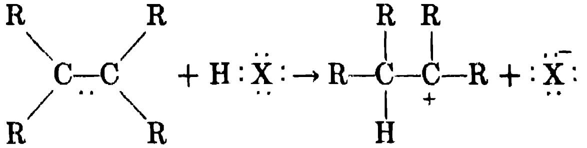
After examining many such reactions, Markownikoff (Markovnikov) noticed that usually one product predominates. He therefore proposed an empirical rule, now known by his name, which states in effect, *when an unsymmetrical molecule adds to an alkene, the negative portion of the addendum* (the substance being added) *will add to the olefinic carbon atom to which there are attached the fewest hydrogen atoms.* Such additions are referred to as *normal additions*, whereas an addition in the opposite manner is an *abnormal addition* or an anti-Markownikoff addition. Thus, in the reaction between HCl and propene, isopropyl chloride is the normal product.

The negative and positive portions of several common substances that add to alkenes with varying readiness are as follows:

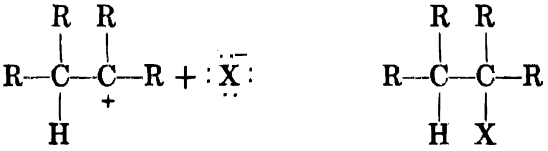
$\overset{+}{\text{H}}\text{—}\overset{-}{\text{OSO}_3\text{H}}$
H—X
X—OH
H—OH
H—R

Observe that hypohalous acids, HOX, ionize in water as H^+ and OX^- but in their behavior toward organic molecules they react with a polarization as $^+X—OH^-$. The addition of hydrocarbons, R—H, requires a strong acid catalyst and will be discussed in the sections on alkylation and polymerization.

The additions proceed by an ionic mechanism. Again, the positive portion of a reagent attacks the alkene to produce a carbonium ion.

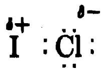


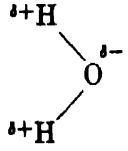
The carbonium ion then reacts with the negative portion of the reagent to form the product.



(7)

When the alkene is unsymmetrical, the time-average position of the mobile electrons is not distributed equally between the two olefinic carbon atoms. The electronegativity of different atoms and groups varies, and this affects the degree of sharing of electrons in covalent bonds. As was explained in Section 1.2, because of differences in electronegativities, i.e., attraction for electrons within a molecule, the shared electrons of a covalent bond spend more of their time nearest the most electronegative atom. This increases the electron density about that atom and decreases it about the other atom to set up a bond dipole.



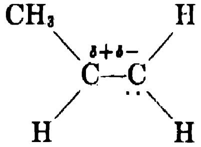


Delta signs are frequently used to indicate fractional charges, although when they are omitted, it is realized that the charges are not unit charges. When several atoms form a group, the group has an average electronegativity itself, so relative electronegativities have been evaluated for various type groups as well as for atoms.

In addition to electronegativity, there are other electrical effects which contribute to the over-all electron-attracting power of atoms and groups. In the case of alkyl groups attached to multiple bonds (or attached to carbonium carbon atoms) the C—H hyperconjugation effect outweighs the electronegativity effect to give the CH_3 group the greatest over-all electron-releasing ability and the *t*-butyl group the least electron-releasing ability. The resultant electron-withdrawing power of some common atoms and groups, then, is in the order

$$CH_3 < CH_2CH_3 < CH(CH_3)_2 < C(CH_3)_3 < H < I < Br < Cl < F.$$

It is seen that the alkyl groups have less electron-attracting power than a hydrogen atom, and therefore the more hydrogen atoms there are attached to an olefinic carbon atom in comparison to alkyl groups, the greater will be the pull on the *mobile* electrons toward that carbon atom. This gives an electron distribution in propene, for example, as follows:



A basis for Markownikoff's rule is apparent. The olefinic carbon atom with the most hydrogen atoms attached has the greater electron density or negative charge, and hence attracts the positive portion of the addendum molecule.

It is to be noticed that this explanation of addition to alkenes is a refinement over Markownikoff's rule. For illustration, in 2-pentene,

$$CH_3—CH_2—CH{=}CH—CH_3,$$

there is an equal number of H's on the olefinic carbon atoms; hence, Markownikoff's rule cannot apply. From the sequence above, however, it is seen that the CH_3 group is more electron-releasing than an ethyl group; consequently the 2-pentene molecule is polarized as

$$CH_3—CH_2—\overset{\delta-}{C}H{=}\overset{\delta+}{C}H—CH_3$$

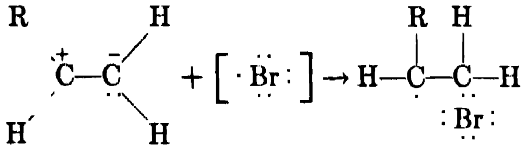
from which one could predict that the addition of HCl would give chiefly 2-chloropentane, which is indeed the case.

The peroxide effect. Kharasch found that in the presence of oxygen or peroxides, HBr adds contrary to the Markownikoff rule. This abnormality is due to a difference in mechanism. A peroxide is a ready source of free radicals, and these react with HBr to liberate bromine atoms.

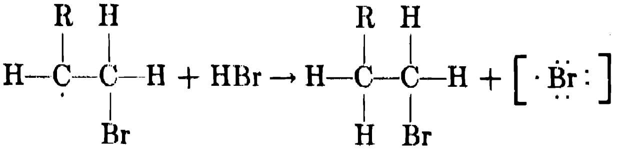
$$R—O—O—R \rightarrow 2[RO\cdot]$$

$$[RO\cdot] + H:\ddot{\underset{\cdot\cdot}{Br}}: \rightarrow RO:H + \left[\cdot\ddot{\underset{\cdot\cdot}{Br}}:\right]$$

The bromine atom seeks an electron vigorously and reacts with that ethylenic carbon atom having the greatest electron density.



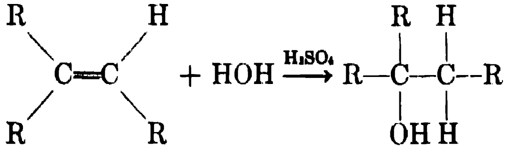
The other ethylenic carbon atom now reacts with a second HBr molecule to yield the product and liberate another bromine atom for perpetuating the reaction.



$$\begin{array}{c}R\ \ H\\ |\ \ \ |\\ H{-}\dot{C}{-}C{-}H\\ \ \ \ |\\ \ \ \ Br\end{array} + HBr \rightarrow \begin{array}{c}R\ \ H\\ |\ \ \ |\\ H{-}C{-}C{-}H\\ |\ \ \ |\\ H\ \ Br\end{array} + [\cdot\ddot{Br}:]$$

The reaction ceases when all the HBr has been used up. This peroxide effect occurs only to a small extent with HCl because of the greater energy required to oxidize a chloride ion to a chlorine atom. On the other hand, HI is immediately oxidized to molecular iodine.

c. Hydration. Water adds to the double bond in the presence of sulfuric acid according to Markownikoff's rule:



A convenient way to hydrate an alkene in an anti-Markownikoff direction is through the *hydroboration* reaction:[3]

$$R{-}CH{=}CH_2 \xrightarrow{NaBH_4{-}AlCl_3} \tfrac{1}{3}(RCH_2CH_2)_3B \xrightarrow[0^\circ]{H_2O_2,\ OH^-} R{-}CH_2{-}CH_2OH$$

This reaction is used often as a way of converting an alkene to an alcohol in a multistep synthesis. Furthermore, if the intermediate hydroboration product is heated for an hour or so in the refluxing diglyme solvent (dimethyl ether of diethyleneglycol) prior to oxidation with the hydrogen peroxide, isomerization will occur such that the boron becomes attached to the least hindered carbon atom. Oxidation would then result in an alcohol with the OH group attached to this carbon. For example,

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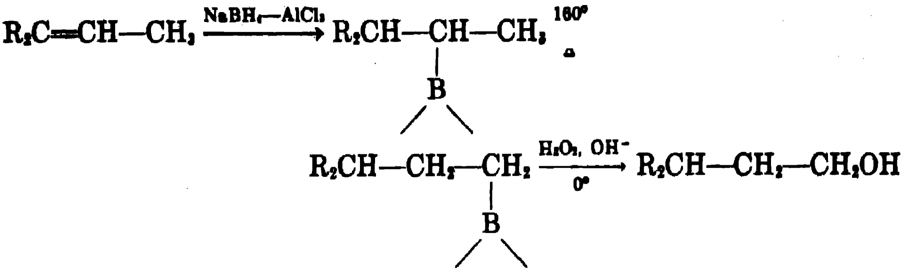
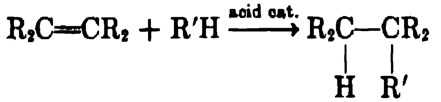
[3] H. C. Brown, *Hybroboration*, W. A. Benjamin, Inc., New York, 1962.



Thus, if it were desired to transform an alkene into a primary alcohol but the alkene is not a 1-alkene, this combined isomerization and hydration reaction would be useful.

d. Alkylation. The addition of an alkane to an alkene is called *alkylation.* The general equation can be written

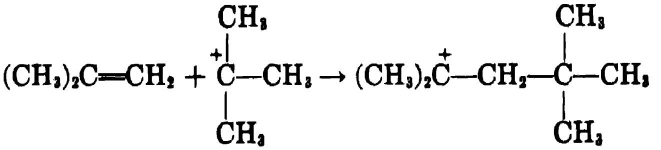


$$R_2C{=}CR_2 + R'H \xrightarrow{\text{acid cat.}} \underset{H}{R_2C}{-}\underset{R'}{CR_2}$$

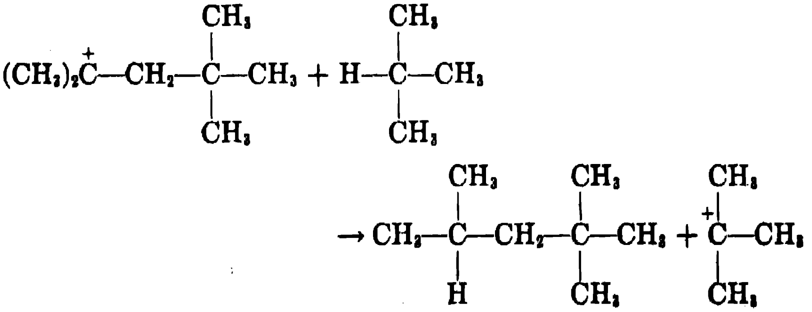
acid cat. = H_2SO_4, H_3PO_4, HF, BX_3, etc.

The action of Lewis acids, e.g., BX_3, is promoted by a proton source such as an alcohol or water molecule. This reaction is an important process in the petroleum industry whereby *alkylate gasoline* is produced by the addition of isobutane to isobutene.

$$(CH_3)_2C{=}CH_2 \xrightarrow{H^+} (CH_3)_2\overset{+}{C}{-}CH_3 \qquad (8)$$



$$(CH_3)_2C{=}CH_2 + \overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{\overset{+}{C}}}{-}CH_3 \rightarrow (CH_3)_2\overset{+}{C}{-}CH_2{-}\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}{-}CH_3 \qquad (9)$$



$$(CH_3)_2\overset{+}{C}{-}CH_2{-}\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}{-}CH_3 + H{-}\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}{-}CH_3$$

$$\rightarrow CH_3{-}\overset{\displaystyle CH_3}{\underset{\displaystyle H}{C}}{-}CH_2{-}\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}{-}CH_3 + \overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{\overset{+}{C}}}{-}CH_3 \qquad (10)$$

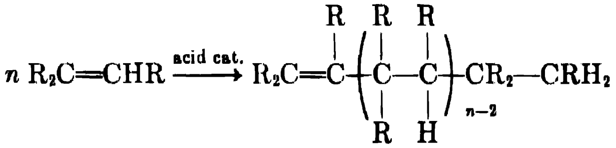
2,2,4-Trimethylpentane
(isooctane)

Then, (9) and (10) are repeated. In reactions (8) and (9) the mode of addition is in the direction to give the most stable carbonium ion (cf. Section 10.6). Equation (10) consists of an abstraction of a hydride ion from the alkane molecule by a carbonium ion.

e. Polymerization. We have seen in Equations (4)–(10) that a carbonium ion may

1. lose a proton to form an alkene,
2. rearrange to a different carbonium ion,
3. combine with a negative ion or a basic molecule to form an alkyl halide, alcohol, etc., or
4. abstract a hydride ion from an alkane molecule.

When the basic molecule in 3. is an alkene, a larger carbonium ion is produced, as in Equation (9). Repetition of this reaction leads to the formation of a large carbonium ion which, when it loses a proton to terminate chain propagation, becomes a multiple of the initial alkene.



$$n\,R_2C{=}CHR \xrightarrow{\text{acid cat.}} R_2C{=}\overset{R}{C}\left(\overset{R}{\underset{R}{C}}-\overset{R}{\underset{H}{C}}\right)_{n-2}CR_2{-}CRH_2$$

This process is called *polymerization:* the formation of a large molecule by the repeated addition of small molecules. The root of the word is from the Greek *meros*, part; hence, *monomer* is one part, *dimer*, two parts or units, and *polymer*, many parts. For example, the gas ethylene polymerizes in the presence of a catalyst to produce a high-molecular-weight polymer, polyethylene, which is a tough, solid substance melting near 118°. It is used for making, among many other things, plastic containers for hydrofluoric acid.

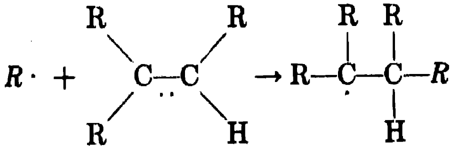
Polymerization proceeds by the addition of the chain to the monomer molecules rather than many small molecules (dimers, trimers, etc.) coupling to form the polymer. In other words, the chain is formed link by link. If a mixture of alkenes is used, then a heterogeneous polymer is produced. Actually, the reaction may be catalyzed by acids, bases, or free radicals. In peroxide or free radical catalyzed polymerization, the odd electron on the catalyst pairs up with one of the *mobile* electrons of the alkene to produce a carbon free radical.

$$(RCO_2)_2 \rightarrow 2RCO_2\cdot$$

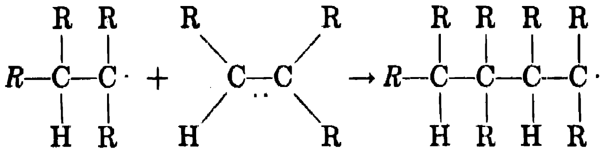
Small quantity of acyl peroxide — **Acyl free radical**

$$RCO_2\cdot \rightarrow R\cdot + CO_2$$

Alkyl free radical



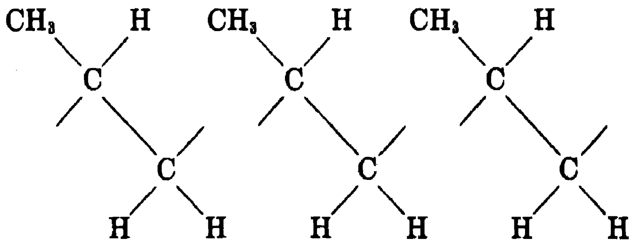
The latter free radical can now react with other free radicals, but since alkene molecules are present in concentration several hundredfold greater than the catalyst, reaction occurs with an alkene molecule to produce a dimer.



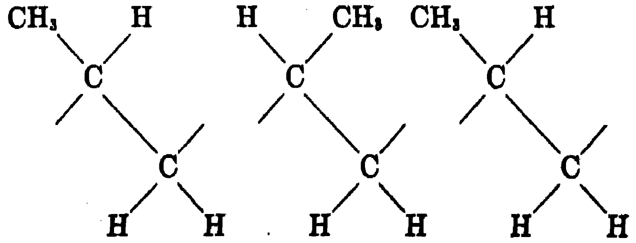
The chain is thereby perpetuated to produce a long polymer. The process is terminated by two free radicals pairing up, or by a free radical taking a hydrogen atom from another molecule. In the latter case, called *chain transfer*, a new free radical chain is started.

One of the most profitable renovations in polymer chemistry was the discovery and development of the transition metal alkyls as catalysts. Karl Ziegler in Germany first discovered their ability to promote the formation of long-chain polymers at low pressures and Giulio Natta in Italy developed their use for the formation of stereo homogeneous polymers. They shared the 1963 Nobel Award in Chemistry for their work. One of the first very successful products of this new synthetic method is *isotactic* polypropylene (e.g. Hercules' *Herculon*). An isotactic polymer is one in which the polymer molecules have a symmetrical structure. This allows the linear molecules to pack closely and gives a crystalline, high-melting fiber. Atactic polypropylene, for example, is a soft, rubbery material.

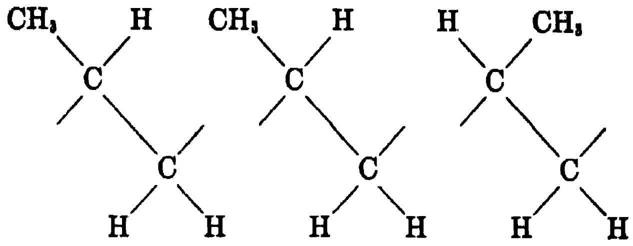
Isotactic polypropylene
(methyls all on same side of chain)



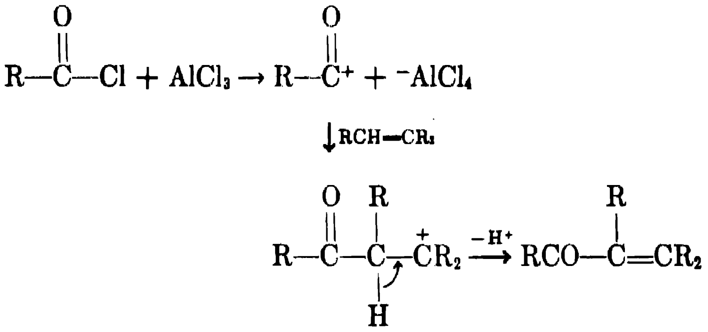
Syndiotactic polypropylene
(methyls on alternating sides of chain).



Atactic polypropylene (methyls randomly located on sides of chain).



f. Acylation. Alkenes undergo a substitution reaction with acyl halides, R—COCl, in the presence of Lewis acids. The mechanism has not been established, but a likely possibility is



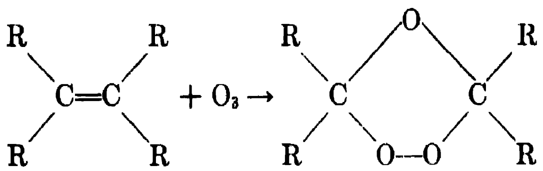
$$\mathrm{R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}Cl + AlCl_3 \rightarrow R{-}\overset{\overset{\displaystyle O}{\|}}{C}{}^{+} + {}^{-}AlCl_4}$$

$$\big\downarrow \mathrm{RCH{=}CR_2}$$

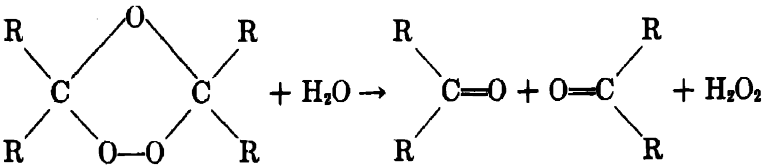
$$\mathrm{R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}\underset{\underset{\displaystyle H}{|}}{\overset{\overset{\displaystyle R}{|}}{C}}{-}\overset{+}{C}R_2 \xrightarrow{-H^+} RCO{-}\overset{\overset{\displaystyle R}{|}}{C}{=}CR_2}$$

A competing reaction is the acid-catalyzed polymerization of the alkene.

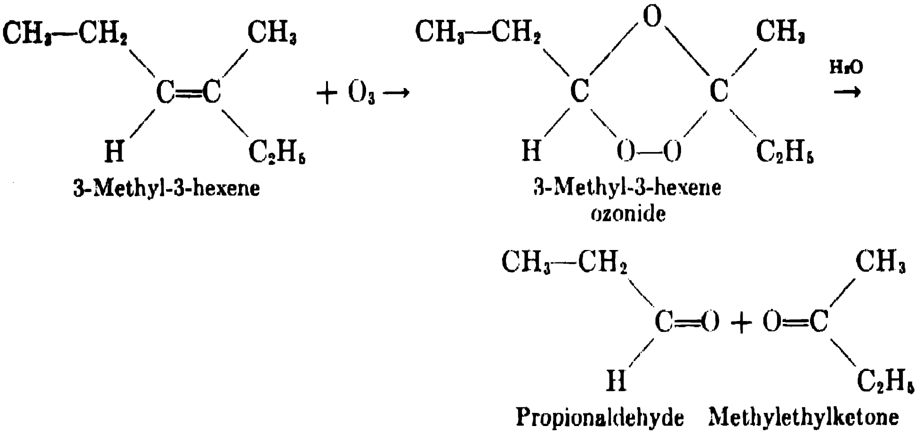
g. Ozone. Ozone vigorously attacks alkenes to produce unstable and sometimes explosive intermediates called *ozonides.*



This is a very useful reaction, because the ozonide can be hydrolyzed without isolation to yield two carbonyl compounds which, if identified, will reveal the structure of the original alkene.



The hydrolysis is carried out in the presence of a reducing agent, such as zinc plus acetic acid or hydrogen plus catalyst, to reduce the hydrogen peroxide as it is liberated. Otherwise the H_2O_2 will oxidize the carbonyl compounds, thereby preventing their isolation and subsequent identification. To illustrate the application of this reaction, suppose it were desired to learn the position of the double bond in a given alkene ($CH_3—CH_2—CH{=}C(CH_3)—C_2H_5$). When this alkene is reacted with ozone and the resulting ozonide hydrolyzed, it would yield the following two carbonyl compounds, which can be identified through methods to be learned later:



3-Methyl-3-hexene

3-Methyl-3-hexene ozonide

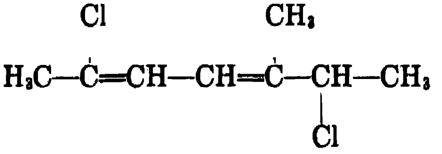
Propionaldehyde Methylethylketone

It was chiefly through the use of this reaction that the structure of natural rubber was determined (see Section 3.6).

The ozonide may be reduced with $LiAlH_4$ or sodium borohydride to yield the corresponding alcohols. If the alcohols are isolated and identified, they too may serve to indicate the position of the double bond in the original alkene. Of course, both reactions may be used not only for structure determination but as ways of preparing carbonyl compounds or alcohols from the respective alkenes. This application as a step in a multistep syntheses will be made later.

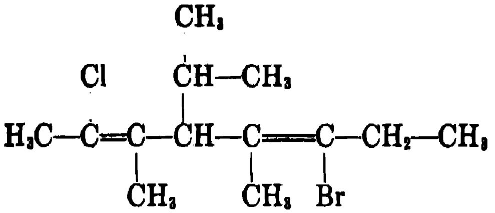
3.5 ALKADIENES

Compounds whose structures contain two C═C bonds are called *alkadienes* or *diolefins*. According to the Geneva system, the class ending is *-diene*, and numerical prefixes indicate the positions of the two double bonds. For example, the structure of 2,6-dichloro-5-methyl-2,4-heptadiene is



$$H_3C—\overset{Cl}{\overset{|}{C}}{=}CH—CH{=}\overset{CH_3}{\overset{|}{C}}—\underset{\underset{Cl}{|}}{CH}—CH_3$$

and the name of the compound having the structure



$$H_3C-\underset{}{\overset{Cl}{C}}=\underset{CH_3}{C}-\overset{CH_3-CH-CH_3}{CH}-\underset{CH_3}{C}=\underset{Br}{C}-CH_2-CH_3$$

is 2-chloro-3,5-dimethyl-4-isopropyl-6-bromo-2,5-octadiene.

There are three relative positions which the two double bonds of an alkadiene may have: both attached to one carbon atom, separated by a single bond, or separated by more than one single bond. These three positions are referred to as *cumulated*, *conjugated*, and *nonconjugated* or *isolated*.

$CH_3-CH=C=CH-CH_3$
Cumulated double bonds

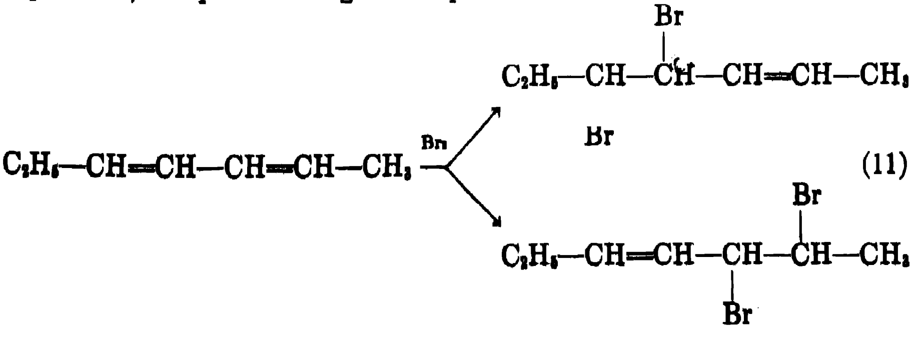
$CH_2=CH-CH=CH-CH_3$
Conjugated double bonds

$CH_2=CH-CH_2-CH=CH_2$
Isolated double bonds

The cumulated structure is the least stable, and frequently the compound will isomerize to an alkyne (see Chapter 4) or to the conjugated diene. The conjugated structure is the most stable, and if there is a possibility of either the conjugated or isolated structures being formed in a reaction, usually the conjugated isomer is the one that results.

The alkadienes undergo the same reactions as do the alkenes, although the former are more reactive and may add two moles of a reagent because of the presence of two double bonds. The simplest alkadiene is allene, $CH_2=C=CH_2$, in which the double bonds are cumulated. One general method of preparing allene hydrocarbons is by dehalogenation of dihalides of the type $R_2C=CBr-CR_2Br$. They have no particular importance, so little need be said about them.

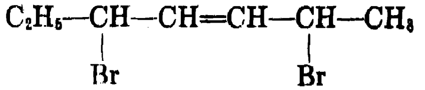
When double bonds are conjugated, addition takes place in an unexpected manner. If one mole of bromine were allowed to react with one mole of 2,4-heptadiene, two products might be expected.



(11)

Instead of either of these two compounds being formed, a different compound is produced:

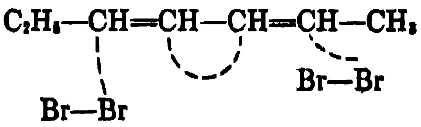
$C_2H_5{-}CH{=}CH{-}CH{=}CH{-}CH_3 + Br_2 \rightarrow$



$$C_2H_5{-}\underset{\displaystyle Br}{\underset{|}{CH}}{-}CH{=}CH{-}\underset{\displaystyle Br}{\underset{|}{CH}}{-}CH_3 \qquad (12)$$

Notice that in equation (12) bromine atoms have added to carbon atoms 2 and 5, breaking both double bonds, and a new double bond has arisen between carbon atoms 3 and 4. This mode of addition is called *1,4-addition*. It means that addition took place at the first and fourth carbon atoms of the conjugated portion of the molecule. These are not the first and fourth carbon atoms in the whole molecule, although they may be, as they would be in pentadiene-1,3. The numbers merely refer to the atoms in conjugation, or what is thought of as the conjugated system. Addition to a double bond as in equation (11) is denoted as 1,2-addition, i.e., addition to adjacent atoms. Of course, if a second mole of addendum is used, then it adds to the remaining double bond as usual.

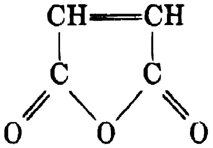
An early attempt to explain 1,4-addition was made by Thiele, in *Thiele's partial valence theory*. He held that an atom forming a multiple bond has not used up all its combining power and has a partial valence reaching out in space like an electrically charged hair. When two multiple groups are conjugated, the partial valences on the atoms separated by the single bond neutralize each other, leaving the 1 and 4 atoms with partial valences waving around freely. When another molecule capable of reacting with the diene approaches the diene, the 1 and 4 carbon atoms of the conjugated system react very easily. For example, the addition of one mole of bromine to one mole of 2,4-heptadiene could be pictured as follows:



All at once several things may happen. The 1 and 4 carbon atoms begin to form covalent bonds with bromine atoms, the Br—Br bonds become weakened and begin to break, the C═C bonds begin to break, and the neutralized partial valences (between the 2 and 3 carbon atoms) begin to change into a normal covalent bond. Finally, the situation arrives in which 1,4-addition has occurred and the isolated bromine atoms can combine with other bromine atoms or react with other heptadiene molecules. This is an oversimplified, slow-motion picture of the reaction. An explanation of 1,4-addition in modern-day language will be given after the theory of resonance has been taken up, although the basic concepts are not greatly different.

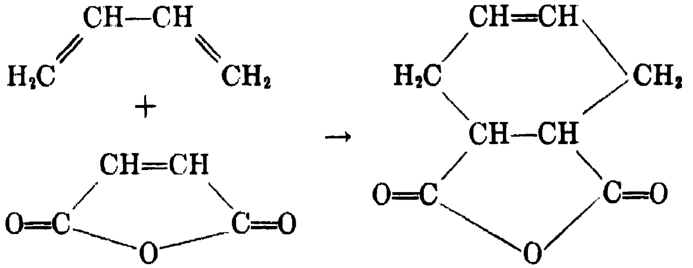
It is to be realized that Markownikoff's rule and 1,4-addition are not followed 100 per cent in practice. Normally the major portion of a reaction will go in accordance with these principles and the other minor products will be lost during purification steps of the chief product. For practical purposes, one may assume that only the 1,4-addition product is formed, although in theoretical studies, the relative amounts of both products would have to be considered.

Conjugated systems undergo a unique reaction, namely, the 1,4-addition of ethylenic bonds which are activated by electron-withdrawing groups. A common substance of this type, called a *dienophile,* is maleic anhydride.



Maleic anhydride

The C=C bond has two carbonyl groups $\left(\rangle C{=}O \right)$ attached. As a result of such activation, the C=C bond adds 1,4 to a conjugated system merely by mixing the reactants in an inert hydrocarbon or ether solvent:



This reaction is known as the *Diels-Alder*[4] *reaction.* It is useful for making a wide variety of products, and particularly for confirming or detecting the presence of a conjugated system. Reference will be made to it on several occasions later in this book.

3.6 THE STORY OF RUBBER

Inasmuch as most rubber products today are synthesized from alkene derivatives, the story of rubber will be told in this chapter. Few people realize the extensiveness of the rubber industry and the important role played by rubber in our daily lives. It is used in thousands of ways in both homes and factories. For instance, rubber parts number over 500 separate items in a modern car and over 20,000 in a battleship. Engine supports, hose, floor mats, brake boots, oil seals, and weather strips are only a few of the major uses on a car. The large companies each manufacture over 30,000 industrial rubber products.

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[4] Otto Diels and Kurt Alder, German chemists, received the Nobel Award in chemistry in 1950.

In 1941 Japan obtained control of the source of over 90 per cent of the U.S. supply of rubber. At that time only 8000 tons of synthetic rubber were being produced, in comparison with a consumption of over half a million tons. The rapid, tremendous growth of the American synthetic-rubber industry from 8000 tons in 1941 to over a million tons in 1945 is one of the greatest chemical engineering achievements of all time, second only to the atomic-bomb project.

a. History.

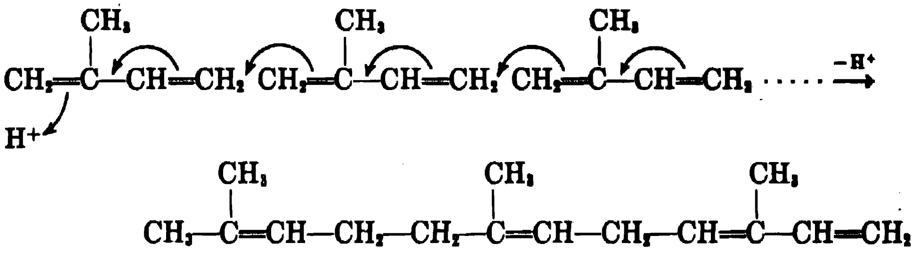
1521—Spanish explorers observed natives playing with rubber balls in Mexico.
1770—Joseph Priestly discovered that caoutchouc would erase pencil marks, so he called it *rubber*.
1819—Macintosh produced a rubberized raincoat, which melted and was sticky in summer and brittle in winter.
1838—Vulcanization discovered by Goodyear and Hancock independently.
1860—Williams decomposed rubber to produce isoprene.
1879—Bouchardat polymerized isoprene to get rubberlike resin.
1882—Tilden determined structure of isoprene.
1914—Germans synthesized inferior grade of rubber.
1930—Thiokol, first commercial synthetic rubber in the United States.
1931—Neoprene, first American general-purpose synthetic rubber commercialized.
1942—American synthetic-rubber industry expanded to exceed prewar natural-rubber consumption.
1949 to present—Synthetic rubber holds major share of rubber industry.

b. Sources of natural rubber. Natural rubber occurs as latex in the cell system between the outer bark and the cambium and in the leaves of many tropical trees and smaller plants. A narrow groove is cut around the tree about 4–5 feet above the ground. The channel is lowered about once a month and by the time the cuts are close to the ground, bark has grown over the original cuts. Some trees have yielded rubber continuously for thirty years. Production centers are Mexico, Liberia, South America, India, and the East Indies.

c. Nature of natural rubber. Latex is a suspension of small rubber globules in water that has a milky appearance. Common practice is to add dilute acid to coagulate the rubber. This coagulum is then washed, dried, and passed through rollers to produce cheeselike sheets called *crepe*. The latex consists of 90–95 per cent of the rubber hydrocarbon called *caoutchouc* (South American Indian word for "weeping tree") and 5–10 per cent impurities (organic acids, sugars, resins, and nitrogenous substances). The crepe is sticky, thermoplastic, elastic over only short temperature ranges, and swells readily in organic solvents.

d. Structure. The fact that destructive distillation of rubber gave isoprene, $CH_2{=}C(CH_3){-}CH{=}CH_2$, and that heating isoprene with HCl gave a rubberlike material, led chemists to the belief that rubber is built up in some way from isoprene units. Natural rubber molecules have an average molecular weight of 1,000,000. Chemical experiments show that rubber contains double bonds, adds halogens, resists hydrogenation, and reacts with ozone. The German chemist C. Harries used ozone to identify the structure of rubber and concluded that it is formed by a 1,4-addition polymerization of isoprene.

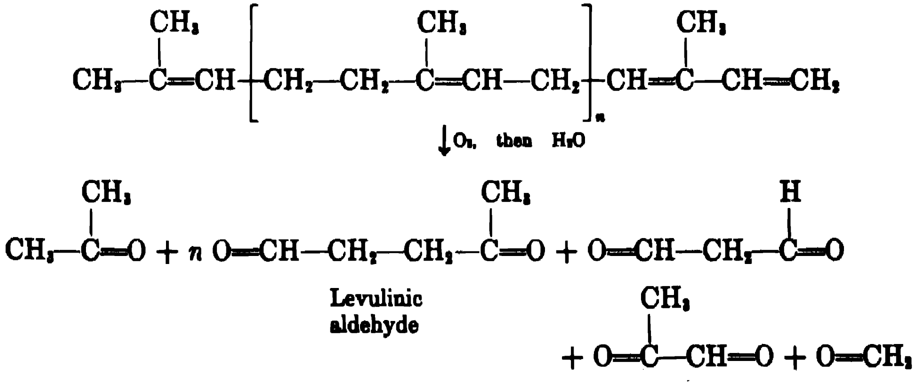
(n + 2) moles



$$\underset{H^+}{CH_2}{=}\overset{CH_3}{\overset{|}{C}}{-}CH{=}CH_2\ CH_2{=}\overset{CH_3}{\overset{|}{C}}{-}CH{=}CH_2\ CH_2{=}\overset{CH_3}{\overset{|}{C}}{-}CH{=}CH_2 \cdots\cdots \xrightarrow{-H^+}$$

$$CH_3{-}\overset{CH_3}{\overset{|}{C}}{=}CH{-}CH_2{-}CH_2{-}\overset{CH_3}{\overset{|}{C}}{=}CH{-}CH_2{-}CH{=}\overset{CH_3}{\overset{|}{C}}{-}CH{=}CH_2$$

Ozonolysis followed by hydrolysis splits the rubber molecule at the double bonds.



$$CH_3{-}\overset{CH_3}{\overset{|}{C}}{=}CH\left[CH_2{-}CH_2{-}\overset{CH_3}{\overset{|}{C}}{=}CH{-}CH_2\right]_n CH{=}\overset{CH_3}{\overset{|}{C}}{-}CH{=}CH_2$$

$$\Big\downarrow O_3,\ \text{then}\ H_2O$$

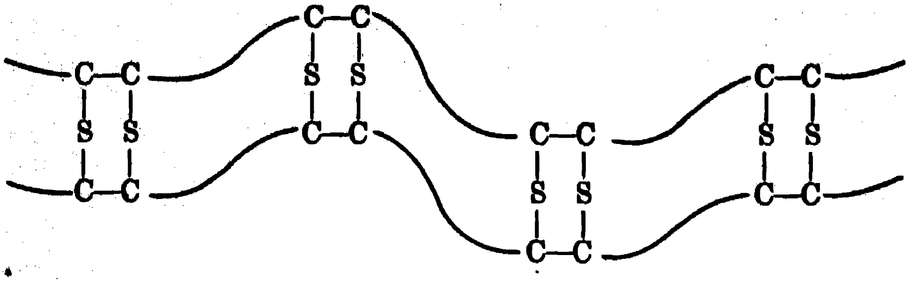
$$CH_3{-}\overset{CH_3}{\overset{|}{C}}{=}O + n\ O{=}CH{-}CH_2{-}CH_2{-}\overset{CH_3}{\overset{|}{C}}{=}O + O{=}CH{-}CH_2{-}\overset{H}{\overset{|}{C}}{=}O$$

$$+\ O{=}\overset{CH_3}{\overset{|}{C}}{-}CH{=}O + O{=}CH_2$$

Levulinic aldehyde

The molecular weight of rubber shows that there are 14,000 isoprene units in the linear chain; hence, n is so large that levulinic aldehyde is practically the only product isolated from the ozonolysis of rubber. Later, X-ray studies confirmed this structure of rubber. Rubber molecules are long chains, twisted spirally, so that the chains uncoil when the rubber is stretched.

e. Vulcanization. The process of curing, called *vulcanization* by Hancock after Vulcan, the Roman god of fire and forge, consists of heating rubber with 3–10 per cent of sulfur at a temperature range of 125–140° for 1–4 hours. Vulcanization is a chemical combination of sulfur with the rubber hydrocarbon. There is a loss of one double bond per sulfur atom combined, forming C—S—C links between polymer chains.



The time and temperature of curing is decreased by catalysts (accelerators) such as amines, and this is made more effective by adding ZnO. The vulcanized product is less sensitive to temperature changes, has greater tensile strength and elasticity over a wider temperature range, and swells less in solvents than does crepe. The elasticity is 700–900 per cent. If 30–50 per cent of sulfur is used, a hard rubber or *ebonite* results. Oxygen attacks rubber slowly, forming acidic and oxygenated substances. Antioxidants are added to retard this deterioration.

f. Processing of rubber. Some rubber products are dipped in a latex mix, then vulcanized, but most rubber products are manufactured out of rubber which is already vulcanized. The latex mix consists of fillers (dyes, wax, etc.), lampblack (for toughness, as required for tires), antioxidants (amines, phenols), softening agents, accelerators, emulsifying agents (soaps), sulfur, asbestos (if fire-resistant product is desired), and the rubber base.

g. Rubber substitutes.

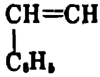
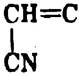
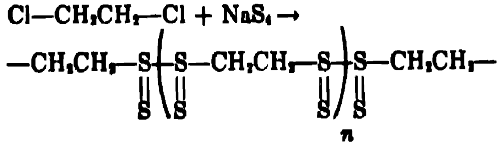
Balata and gutta-percha: These are stereoisomers of natural rubber (see page 124). They are not very elastic, are tough, and are thermoplastic.

Reclaimed rubber: Rubber goods are ground, treated with alkali or acid to remove fabrics, then washed, dried, and compounded with new rubber. Reclaimed rubber has only 300–400 per cent elasticity.

Synthetic rubber: When the Allies imposed a shipping embargo on Germany during World War I, Germany had to find a new source of rubber. Isoprene production from turpentine and other sources was limited, but they found that polymerization of 2,3-dimethylbutadiene produces a rubberlike mass. The dimethylbutadiene was easily produced from acetone. The polymerization was catalyzed by sodium in a CO_2 atmosphere and given the name *buna rubber*. It was a very inferior product and its production ceased after the war.

Research on the synthesis of rubber continued slowly; but in 1941, when Japan cut off the availability of rubber from the East Indies where the United States was getting 90 per cent of its supply, research and production of synthetic rubber suddenly grew into a mammoth industry. Soon five major types of rubber were developed, among which either one or another is as good or better than natural rubber for any purpose except for truck tires. For instance, butyl rubber is far superior for inner tubes; buna N rubber is best for fuel lines at the extremely cold temperatures of arctic countries; and some synthetic rubbers do not burn or carry a flame. The price of natural rubber fluctuates a great deal because of labor problems and competition, but in general the prices of natural and synthetic rubber are comparable.

TABLE 3.3. FIVE GENERAL TYPES OF SYNTHETIC RUBBERS PRODUCED IN THE UNITED STATES ON A COMMERCIAL SCALE

Name	Monomers Used	Chief Use and Characteristics
GR-S, or Buna S	1,3-Butadiene + styrene $CH_2{=}CH{-}CH{=}CH_2$  $\underset{\underset{C_6H_5}{\vert}}{CH}{=}CH_2$	An all-purpose rubber which can replace natural rubber in most of its uses
GR-I, Butyl, Polybutene	Isobutylene $(CH_3)_2C{=}CH_2$	For inner tubes and tubeless tires; many times more resistant to oxidation, and holds air better than natural rubber
Buna N, Perbunan, Hycar, Chemigum	1,3-Butadiene + acrylonitrile $CH_2{=}CH{-}CH{=}CH_2$  $\underset{\underset{CN}{\vert}}{CH}{=}CH_2$	Resistant to oils and cold temperatures: used for self-sealing gas tanks, oil and hydraulic fluid hose, rubber gloves, etc.
Neoprene GR-M,	Chloroprene $CH_2{=}CCl{-}CH{=}CH_2$	Nearest to natural rubber in properties and uses: used for household and medical articles
Thiokol	Ethylene chloride + sodium polysulfide $Cl{-}CH_2CH_2{-}Cl + NaS_4 \rightarrow$  $-CH_2CH_2-\underset{\underset{S}{\Vert}}{S}\left(-\underset{\underset{S}{\Vert}}{S}-CH_2CH_2-\underset{\underset{S}{\Vert}}{S}-\right)_n\underset{\underset{S}{\Vert}}{S}-CH_2CH_2-$	Used for gaskets, seals, pulleys, and hard-rubber products to be exposed to oil and pressure

In Table 3.3 are listed the five general types of synthetic rubbers produced in the United States, of which 75 per cent of the total is GR-S. In Table 3.4 is given the U.S. consumption of rubber in the years of 1944 and 1954. Synthetic rubber production reached 1.5 million *tons* in 1962, with buna S type comprising two-thirds of this.

GR-S, or buna S, rubber is a copolymer of approximately 78 per cent butadiene and 22 per cent styrene (a molar ratio of about 7:1), most of which

TABLE 3.4. UNITED STATES CONSUMPTION OF RUBBER IN LONG TONS

Type	1954	1944
Natural rubber	597,435	144,113
GR-S	483,001	494,115
Butyl	61,314	10,763
Neoprene	57,203	46,243
GR-N	17,115	14,112
Total synthetic	635,977	566,670
Total natural and synthetic	1,233,412	710,783

is polymerized today at relatively low temperatures and by a free-radical catalyst.

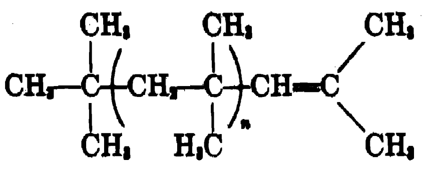
Butadiene is a gas, and styrene boils at 145°. Polymerization gives off a large quantity of heat, so water is added to help control the temperature. Since the hydrocarbons are insoluble in water, soap is added to produce an emulsion. The reaction is carried out in a large closed tank to which is added a peroxide and a modifying agent, and the mixture is stirred at a temperature near 5° for approximately 15 hours. By this time the polymerization is two-thirds completed and an inhibitor is added to destroy the peroxide. The excess butadiene and styrene are removed and recovered, an antioxidant is added, and the synthetic rubber is coagulated with an acidic salt solution, washed, dried, and baled.

Modifiers are certain agents such as higher mercaptans, RSH, which control the growth of the polymer chain. A commonly used inhibitor is hydroquinone.

Sixty-one per cent of all rubber produced in the United States is used to manufacture tires. GR-S is preferred for passenger cars, because it gives 30 per cent longer wear than natural rubber. Rubber gives off heat when stretched, and since it is also a poor conductor, heat accumulates in a tire. Passenger-car tires are now designed to withstand this heat. Only about 10 per cent GR-S can be used satisfactorily in truck tires; *cis*-polybutadiene has proved to be a much better material for truck tires. A typical tread recipe for passenger tire rubber is

	Parts
Synthetic rubber	65.0
Zinc oxide	2.0
Carbon black	23.7
Organic acids	0.5
Process oil	7.0
Sulfur	0.9
Accelerator	0.3
Antioxidant	0.6
	100.0

Butyl rubber is simply polyisobutylene:



where n may be as large as several thousand. Thus butyl rubber is essentially saturated and therefore resistant to oxidation. It cannot be vulcanized, and since vulcanization improves the elasticity of rubbers, the usual formula has 97 parts of isobutylene with 3 parts of isoprene or butadiene polymerized with an acid catalyst like $AlCl_3$ at −100°. Today all inner tubes are manufactured from butyl rubber.

The acrylonitrile content of buna-N type rubber varies from 18 to 45 per cent. Increasing the acrylonitrile content over this range improves the petroleum-oil resistance, tensile strength, and high-temperature resistance but simultaneously reduces the elasticity and low-temperature flexibility of the rubber. The polar rubbers (buna N and neoprene) are more resistant to nonpolar oils (hydrocarbons), whereas nonpolar rubbers (natural rubber and butyl rubber) are more resistant to polar oils (esters of phosphoric acid).

Several other synthetic rubbers are in the pilot-plant stage. One is white, from which tires could be made to match the color of a car; another type

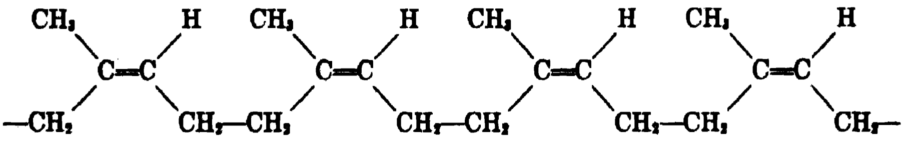
TABLE 3.5. RELATIVE RATING OF DIFFERENT RUBBERS

	Natural Rubber	GR-S	Butyl	Neoprene	Nitrile	Thiokol
Workability	E	G	G	G	G	F
Ease of cure	E	E	G	E	E	F
Adhesion	E	E	G	E	E	F
Strength	E	G	F	G	E	F
Elongation	E	G	E	G	E	F
Aging	G	E	E	E	E	E
Set	E	E	F	G	E	P
Gas diffusion	F	F	E	G	G	E
Food contamination	E	F	G	F	F	F
Electrical resistance	E	E	. . .	F	F	F
Nonflammability	P	P	P	G	. . .	. . .
Resistance to solvents						
Lubricating oil	P	P	P	G	E	E
Aromatics	P	P	F	P	F	G
Chlorinated	P	P	P	P	G	G
Lacquers	P	P	P	P	F	G

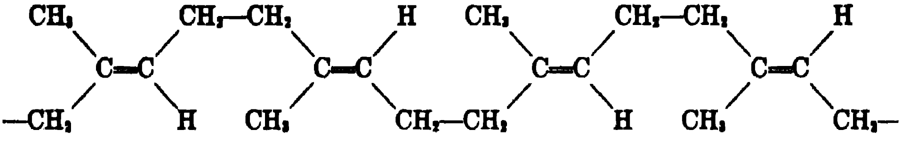
E = excellent; G = good; F = fair; P = poor.

shows swell-resistance to the high-temperature synthetic lubricants; and the "fluororubbers" are *nonflammable. Thus, synthetic rubbers can be made* with a wide variety of remarkable properties, some of which cannot be matched by natural rubber. A comparison of the major rubber types with respect to their important characteristics is given in Table 3.5. From this table it is apparent that the wide variety of applications of rubber in this mechanical age can be met only by the combined availability of the synthetic and natural rubbers.

h. Stereoisomerism among rubbers. When isoprene polymerizes, it can do so to yield an all-*cis*, an all-*trans*, or a mixed *cis-trans* polymer.



All-*cis* polyisoprene structure



All-*trans* polyisoprene structure

Natural rubber has the all-*cis* structure, and gutta-percha and balata have the all-*trans* configuration. Biological reactions are very specific with respect to the spatial shapes of molecules involved. In this case, the hevea, or natural rubber trees, produce one geometric isomer, in spite of the very large molecular size, whereas a different plant produces its geometric isomer, gutta-percha, etc. Until the 1950's, man was not able to polymerize isoprene to produce a replica of natural rubber.[5] The synthetic product always differed sterically, and therefore had different properties. The spatial shape is an important factor; for instance, the elasticity of natural rubber is twice that of its isomer, gutta-percha and balata.

In 1955, several rubber companies announced the synthesis of stereospecific rubbers, such as all *cis*- or all *trans*-1,4-polyisoprene. By 1963, stereo rubbers from polybutadiene and polyisoprene accounted for 9 per cent of all rubber production in the U.S.

The general properties of large molecular weight compounds, or macromolecules, will be discussed in Section 26.4 along with synthetic textiles and plastics.

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[5] It is known that the plant does not polymerize isoprene itself but probably a derivative of β-methyl-crotonic acid, $(CH_3)_2C{=}CH{-}COOH$.

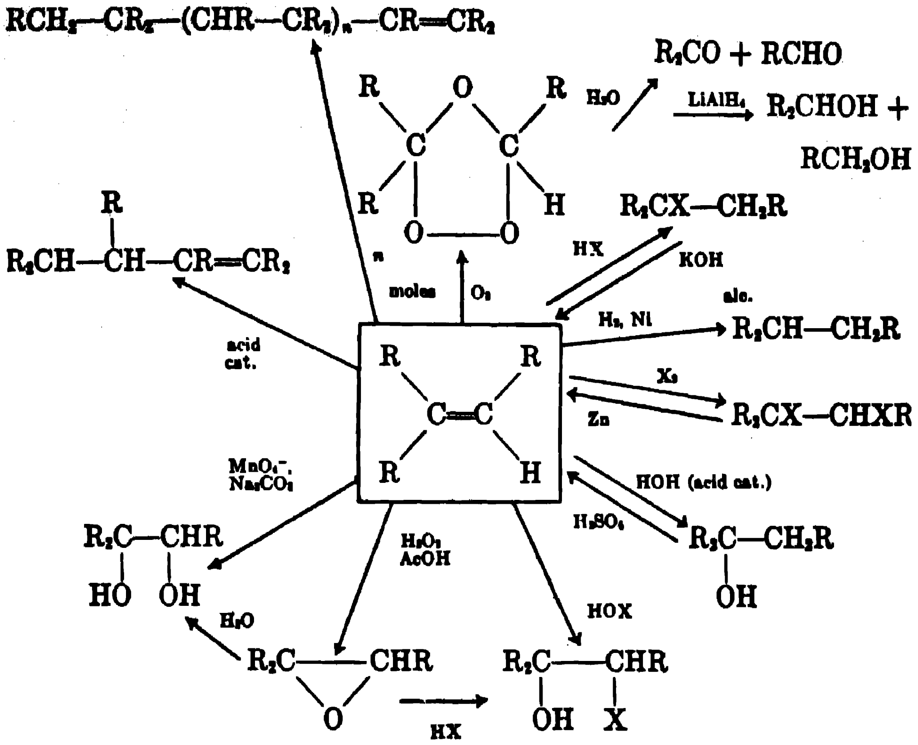


Fig. 3.4. Characteristic reaction chart for alkenes.

STUDY EXERCISES

1. Write equations illustrating four laboratory methods of producing alkenes.

2. How are alkenes produced industrially?

3. How do alkanes and alkenes differ with respect to reduction, oxidation, substitution, and addition reactions?

4. Write structural formulas for the following compounds: (a) 2-methyl-3-hexene, (b) 2-chloro-1,3-pentadiene, (c) 2-methyl-4,4-dichloro-2-hexene, (d) 2-bromo-2,4-hexadiene, (e) 2,3-pentadiene.

5. What reagent and conditions would be used to bring about the following changes?

$CH_3—CH=CH—CH_3 \rightarrow CH_3—CHOH—CHOH—CH_3$
$(CH_3)_2C=CH—C_2H_5 \rightarrow (CH_3)_2CBr—CH_2—CH_2—CH_3$
$CH_3—CH_2—CH=C(CH_3)—C_2H_5 \rightarrow CH_3—CH_2—CHO + C_2H_5—CO—CH_3$

6. State or define the terms (a) polymerization, (b) Markownikoff's rule, (c) 1,4-addition, (d) conjugation, (e) addition reaction, (f) alkylation, (g) isoprene unit.

7. How could 3-heptene be prepared in the laboratory starting with any desired compound?

8. What is Thiele's partial valence theory?

9. How would you convert ethylene into (a) ethylene chloride, (b) ethane, (c) chloroethane, (d) 1-butane, (e) ethylene glycol, (f) ethylene chlorohydrin, (g) ethyl alcohol.

10. Name and give the structural formulas of the isomeric hexenes.

11. Give the name and structural formula of the reaction product when one mole of 1,3-octadiene is treated with one mole of bromine.

12. Show two possible structures for 2-pentene.

13. Give the structure and name of the compound from the normal addition of HCl to (a) trimethylethylene, (b) 1-pentene, (c) 2-pentene, (d) 2-methyl-2-pentene.

14. Write the structural formula and the name of the compound formed when one mole of bromine reacts with one mole of (a) 1-pentene, (b) 2-hexene, (c) 3-heptene, (d) 3-methyl-2-pentene, (e) 3-methyl-1,3-hexadiene, (f) 2,4-dimethyl-2,4-octadiene.

15. Describe rubber latex as obtained from trees.

16. Describe briefly the process of vulcanization.

17. What are several types of substances compounded with rubber in the manufacture of rubber products?

18. What are the monomers used to produce buna S, butyl, neoprene, buna N and Thiokol rubbers? What are special uses or properties of these rubbers?

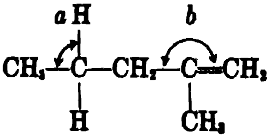
19. Indicate by equations what reactions, if any, would occur when the following substances are mixed and gently warmed:

$$CH_3—CH_2—CHBr—CH_3 \quad + \quad \text{sodium metal} \rightarrow$$
$$CH_3—CH_2—CHBr—CH_3 \quad + \quad KOH_{alc.} \rightarrow$$
$$CH_3—CH_2—CHBr—CH_3 \quad + \quad Zn + HCl_{conc.} \rightarrow$$
$$CH_3—CH_2—CH_2—CH_3 \quad + \quad Zn + HCl_{conc.} \rightarrow$$

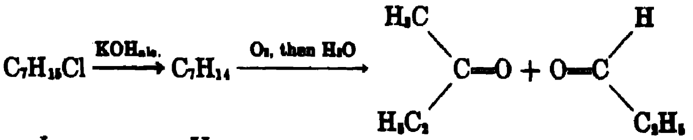
20. Illustrate the acid-catalyzed dimerization and polymerization of 2-methyl-2-butene.

21. When bromine is added to ethylene in methyl alcohol solution, some $Br—CH_2—CH_2OCH_3$ is produced in addition to ethylene bromide. Offer an explanation for the formation of the side product.

22. What are the angles *a* and *b* in the compound



23. On the basis of the following information, deduce the structural formula of I and II:



I II

TEST QUESTIONS, Set 3

1. What should be the principal product when HCl is added to 5-methyl-3-hexene?

2. Give the name and structural formula for the final product when 1,2-dibromohexane is warmed with zinc dust and the reaction product is treated with hydrogen chloride.

3. One mole of 2-hexene was reacted with excess bromine at room temperature to give 100 g of product. What was the per cent yield in the reaction? How many grams of zinc would be needed to reconvert the product into hexene?

4. An olefin was treated with ozone and the resulting ozonide hydrolysed to yield

(CH$_3$—CH$_2$)$_2$C═O plus (CH$_3$)$_2$CH—CHO. What was the structure of the original olefin?

5. What volume of ethylene measured over water at 25° and 740 mm can be obtained from 50 g of alcohol? From 50 kg of alcohol?

6. Illustrate by equations, using structural formulas, two modes of addition of isopentane to isobutylene.

7. Illustrate by equations, using structural formulas, a dimerization of isobutylene to yield an olefin which may be hydrogenated to Isooctane.

8. What volume of propene, STP, can be obtained from 150 g of *n*-propyl bromide if the latter is 82 per cent pure?

9. How could 2-hexene be distinguished from hexane by qualitative test-tube experiments?

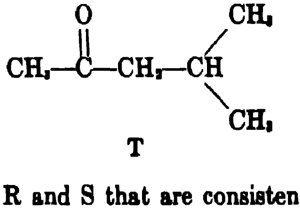
10. A bromine solution in CCl$_4$ is 0.08 molar. What volume will react at room temperature with 0.196 g of 3-methyl-2-hexene?

11. Each of the following preparations involves several combinations of reactions given in this or earlier chapters. Give a sequence of reactions you could carry out *in the laboratory* to perform the transformations indicated. These are called *multistep syntheses.*

(a) *n*-propyl bromide to 1,2-dichloropropane
(b) isopropyl alcohol to *n*-propyl bromide
(c) ethyl bromide to ethylene chlorohydrin
(d) 1-bromo-2-methylbutane to CH$_3$—CH$_2$—CO—CH$_3$
(e) isopropyl bromide to *n*-hexane
(f) 3-methyl-1-butene to 2,3-dimethylbutane

12. A hydrocarbon is known to be either 2-methyl-2-pentene or 3-methyl-2-pentene. What would you do in the laboratory to establish its structure?

13. An alkyl dihalide R (C$_6$H$_{12}$Br$_2$) was treated with excess alcoholic KOH to produce S (C$_6$H$_{10}$). When S is hydrated in the presence of sulfuric acid, compound T is obtained:

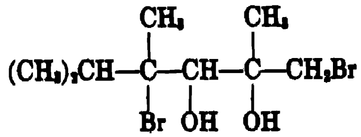


T

Give structural formulas for R and S that are consistent with the facts above and show how you reached your answer.

14. What weight of the appropriate R—Br compound would be required to produce one mole of 5,6-di-(β,β-dimethyl-butyl)-2,8-decadiene by the Wurtz reaction if the reaction took place in an 80 per cent yield?

15. An unsaturated compound W (C$_9$H$_{17}$Br) was treated with alcoholic KOH to produce an alkadiene X (C$_9$H$_{16}$). When X was treated with one mole of bromine, compound Y (C$_9$H$_{16}$Br$_2$) was obtained. Then compound Z



$$(CH_3)_2CH\text{—}\underset{Br}{\overset{CH_3}{C}}\text{—}\underset{OH}{CH}\text{—}\underset{OH}{\overset{CH_3}{C}}\text{—}CH_2Br$$

Z

was obtained by the oxidation of Y with $KMnO_4$ in aqueous Na_2CO_3. Give structural formulas for W, X, and Y that are consistent with the above observations and show how you obtained your answer.

16. What series of laboratory reactions would you use to prepare 2,2,7,7-tetramethyloctane starting with 2,2-dimethyl-3-bromobutane?

4

Alkynes

Alkynes are aliphatic compounds whose structures contain a carbon-carbon triple bond, —C≡C—. They are referred to as *acetylenic compounds*, after the name of the first member of the family, *acetylene*. Molecular formulas of the unsubstituted alkynes fit the general empirical formula, C_nH_{2n-2}.

When an *s* and a *p* orbital of carbon hybridize to form two *sp* hybrid orbitals, the carbon atom may form two molecular orbitals which will be colinear. Two *p* orbitals would be left at the carbon atom, each containing an unpaired electron. Thus, in acetylene, each carbon atom can have two *p* orbitals perpendicular to the axis of the molecule. The *p* orbitals may coalesce to form two pi orbitals perpendicular to each other, but since the two pi orbitals can have any angle about the C—C axis within 360°, this gives a cylindrical pi electron cloud about the C—C axis.

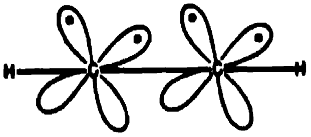


Fig. 4.1.

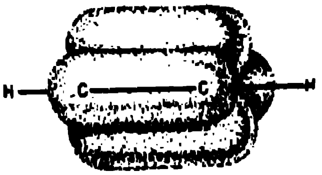
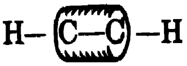
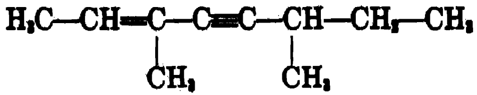


Fig. 4.2. Shape of the pi orbitals in acetylene.



4.1 NOMENCLATURE

The Geneva system of naming alkynes is analogous to that for the alkenes, with the class ending being *-yne* (*-ine*, in the old literature) instead of -ene. Immediately the question arises, what to do about compounds containing a C═C and a C≡C bond? These compounds are named by using the regular suffixes *-ene* and *-yne*, with numbers to indicate their respective positions in the main chain. For example, the name of the compound,



$$H_3C—CH{=}\underset{CH_3}{C}—C{\equiv}C—\underset{CH_3}{CH}—CH_2—CH_3$$

✓ is 3,6-dimethyl-2-octene-4-yne.

4.2 PREPARATION

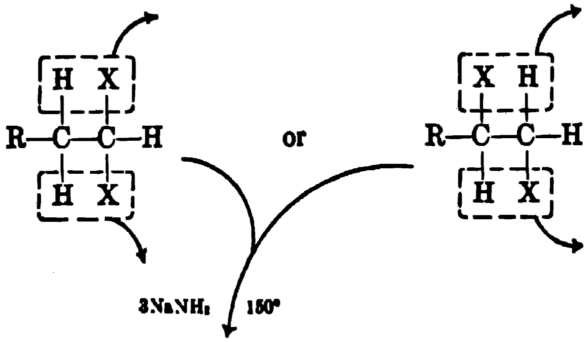
a. Laboratory preparation. Alkynes may be prepared by the same procedures used for alkenes, that is, by forming multiple carbon-carbon bonds in a molecule through the removal of H,X or X,X.

$$R—CH_2—CX_2—R + 2KOH_{alc.} \rightarrow R—C{\equiv}C—R + 2KX + 2H_2O$$

$$R—CX_2—CX_2—R + 2Zn \rightarrow R—C{\equiv}C—R + 2ZnX_2$$

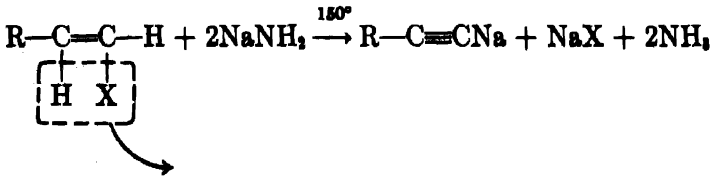
When preparing 1-alkynes, $KOH_{alc.}$ should not be used, because it catalyzes the isomerization of 1-alkynes to 2-alkynes. Instead, sodium amide has been found to give excellent yields. One may use an alkyl dihalide,[1]

geminal (cf. page 327) *vicinal*



$$R—C{\equiv}CNa + 2NaX + 3NH_3$$

or one may use a haloalkene.



$$R—\underset{H}{C}{=}\underset{X}{C}—H + 2NaNH_2 \xrightarrow{150°} R—C{\equiv}CNa + NaX + 2NH_3$$

The sodium alkynide which is ionic, is then hydrolyzed in dilute acid to yield the 1-alkyne.

$$R—C{\equiv}CNa + HCl \rightarrow R—C{\equiv}C—H + NaCl$$

b. Acetylene. A very simple method of preparing acetylene is by the hydrolysis of calcium carbide.

---

[1] When the two halogen atoms are on the same carbon atom they have the *geminal* (gem.) position, and when attached to adjacent carbon atoms the two halogens are in the *vicinal* (vic.) position.

$$CaC_2 + 2HOH \rightarrow Ca(OH)_2 + H—C{\equiv}C—H$$

The method requires no special laboratory equipment other than that for collecting gases, and so this method is commonly used in the elementary organic laboratory course for making acetylene.

c. **Industrial production of acetylene.** Essentially, the same methods are used for preparing alkynes on laboratory and commercial scales. However, the only alkyne of major industrial importance is acetylene. There are two competing methods of producing acetylene: the hydrolysis of calcium carbide and the cracking of petroleum oils. Very little petroleum is found in Germany, but this country has an abundance of coal. Therefore Germany and most of Europe must rely upon coal as a natural carbonaceous resource for building their organic chemical industries. The major routes from coal to aliphatic chemicals are I and II, as shown in Figure 4.3. Today's extensive use of both routes is due to the ingenious pioneering work of German chemists. By route II, acetylene is made from coke, and the cost of acetylene is affected by the demand on coke made by other industries. In the cracking of petroleum oils to produce gasoline, acetylene is one of the gaseous side products. It is also made by cracking ethane or propane.

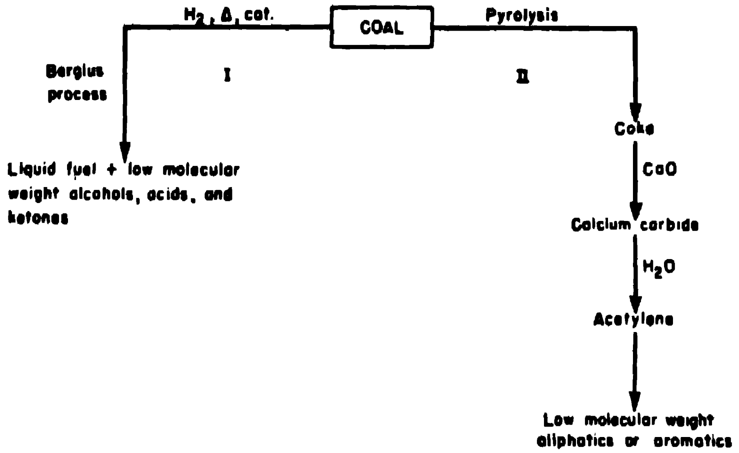

H₂, Δ, cat.
COAL
Pyrolysis
Bergius process
I
II
Coke
Liquid fuel + low molecular weight alcohols, acids, and ketones
CaO
Calcium carbide
H₂O
Acetylene
Low molecular weight aliphatics or aromatics

Fig. 4.3. Major routes from coal to aliphatic chemicals.

4.3 PHYSICAL AND CHEMICAL PROPERTIES

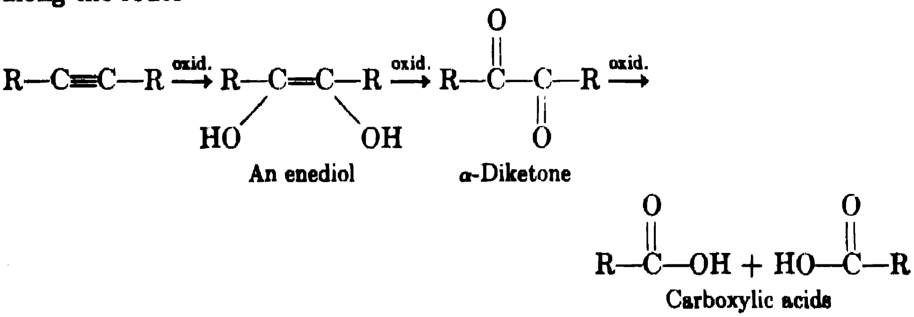
The physical properties of the alkynes show the same trend with increasing molecular weight as found for the other aliphatic hydrocarbons (cf. Table 4.1). The solubilities in water of the alkanes, alkenes, and alkynes are all small, although there is a definite increase in the order named.

The typical reactions of the alkynes are along the same lines as those of the alkenes: namely, they (1) undergo addition reactions in the cold, (2) are

TABLE 4.1. PHYSICAL CONSTANTS OF SOME ALKYNES

Name	Molecular Formula	Melting Point	Boiling Point	Sp. Gr. (liq.)
Acetylene	C_2H_2	−82	−83	0.618
Propyne	C_3H_4	−102	−23	.671
1-Butyne	C_4H_6	−122	9	.668
1-Pentyne	C_5H_8	−98	40	.695
1-Hexyne	C_6H_{10}	−124	72	.719
1-Heptyne	C_7H_{12}	−80	100	.733
1-Octyne	C_8H_{14}	−70	126	.747
1-Nonyne	C_9H_{16}	−65	151	.763
1-Decyne	$C_{10}H_{18}$	−36	182	.770
2-Butyne	C_4H_6	−24	27	.694
2-Pentyne	C_5H_8	−101	55	.714
2-Hexyne	C_6H_{10}	−92	84	.730

easily oxidized, and (3) are catalytically polymerized. These are the characteristic features of unsaturated compounds. The oxidation of alkynes is along the route


$$R{-}C{\equiv}C{-}R \xrightarrow{\text{oxid.}} \underset{\text{An enediol}}{R{-}\underset{HO}{C}{=}\underset{OH}{C}{-}R} \xrightarrow{\text{oxid.}} \underset{\alpha\text{-Diketone}}{R{-}\overset{O}{\overset{\|}{C}}{-}\underset{O}{\underset{\|}{C}}{-}R} \xrightarrow{\text{oxid.}} \underset{\text{Carboxylic acids}}{R{-}\overset{O}{\overset{\|}{C}}{-}OH + HO{-}\overset{O}{\overset{\|}{C}}{-}R}$$

The enediol is rarely isolable; the diketone is sometimes isolable, usually the two acids are the products recovered. Notice that identification of the two acids reveals the structure of the original alkyne.

a. Metal alkynides. There is one qualitative difference between the reactivities of alkenes and alkynes, and that is the acidity of the alkynes. The hydrogen atom attached to the acetylenic carbon atom in 1-alkynes, R—C≡C—H, is active enough to be replaceable by metal ions. Two classes of metal alkynides are obtained. One type, like those with cuprous and silver ions, is fairly covalent, insoluble, and unaffected by water; the second type, like those with sodium ion, is ionic and is rapidly hydrolyzed by water. The cuprous and silver alkynides can be prepared in aqueous ammonia by merely mixing ammoniacal solutions of the salts and a 1-alkyne.

$$R{-}C{\equiv}C{-}H + Ag(NH_3)_2^+ \rightarrow R{-}C{\equiv}C{-}Ag + NH_4^+ + NH_3$$
$$R{-}C{\equiv}C{-}H + Cu(NH_3)_2^+ \rightarrow R{-}C{\equiv}C{-}Cu + NH_4^+ + NH_3$$

The alkynides precipitate and are fairly stable while wet; but they are explosive when dry. Acetylene will give also the dimetal salts, $\mathrm{Ag{-}C{\equiv}C{-}Ag}$ or $\mathrm{Cu{-}C{\equiv}C{-}Cu}$. The alkynes may be recovered from the salts by treatment with dilute mineral acids.

$$\mathrm{R{-}C{\equiv}C{-}Ag + HCl \rightarrow R{-}C{\equiv}C{-}H + AgCl}$$

The sodium alkynides are best prepared from the 1-alkyne plus sodium amide in liquid ammonia, although sodium metal may be used.

$$\mathrm{R{-}C{\equiv}C{-}H + NaNH_2 \rightarrow R{-}C{\equiv}C^{-}Na^{+} + NH_3}$$

The sodium alkynides are salts of extremely weak acids; hence, they hydrolyze readily when in contact with water to liberate the 1-alkyne.

$$\mathrm{R{-}C{\equiv}CNa + HOH \rightarrow R{-}C{\equiv}C{-}H + NaOH}$$

This reaction is not reversible to any significant degree; that is, as strong a base as sodium hydroxide is, the 1-alkyne is too weak an acid for the two to give even detectable amounts of the sodium alkynide. On a basis of the rule of thumb that *stronger acid liberates weaker acid, and stronger base liberates weaker base from their salts*, this reaction implies that HOH is a stronger acid than a 1-alkyne, or that a sodium alkynide is a stronger base than NaOH. Both implications are true. Throughout this book several substances will be given which are stronger bases than NaOH.

The activity of the acetylenic hydrogen in 1-alkynes is revealed by another reaction. It will be recalled that Grignard reagents react with substances having active hydrogens (essentially, these are hydrogens replaceable by metals), and the acetylenic hydrogens of 1-alkynes are sufficiently active to react with Grignards.

$$\mathrm{R{-}C{\equiv}C{-}H + R'MgX \rightarrow R'{-}H + R{-}C{\equiv}CMgX}$$

Thus, the alkyne Grignard can easily be prepared. Alkyne Grignards and sodium alkynides react with alkyl halides to give disubstituted acetylenes.

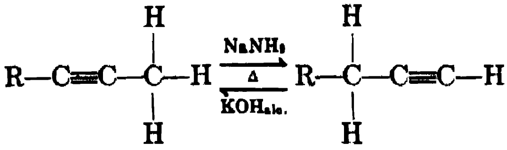
$$\begin{array}{lcl} \mathrm{R{-}C{\equiv}CMgX} & & \mathrm{+\ MgX_2} \\ \quad\text{or} & \mathrm{+\ R'X \rightarrow R{-}C{\equiv}C{-}R'} & \quad\text{or} \\ \mathrm{R{-}C{\equiv}CNa} & & \mathrm{+\ NaX} \end{array}$$

One useful application of such a reaction is the lengthening of a chain of carbon atoms, one carbon at a time. The metal alkynide is allowed to react with methyl bromide first. For simplicity, only the sodium alkynide will be used in an illustration, although the alkyne Grignard will do as well.

$$\underset{\mathrm{I}}{\mathrm{R{-}C{\equiv}C{-}H}} + \mathrm{NaNH_2 \rightarrow R{-}C{\equiv}CNa + NH_3}$$

$$\mathrm{R{-}C{\equiv}CNa + CH_3Br \rightarrow R{-}C{\equiv}C{-}CH_3 + NaBr} \qquad (1)$$

Under the influence of catalytic amounts of sodium amide, 2-alkynes isomerize to 1-alkynes, whereby two hydrogen atoms migrate from the one-carbon to the three-carbon atom, and two C—C bonds shift toward the end of the chain.



$$R-C\equiv C-\overset{H}{\underset{H}{\overset{|}{\underset{|}{C}}}}-H \underset{KOH_{alc.}}{\overset{NaNH_2}{\underset{\Delta}{\rightleftharpoons}}} R-\overset{H}{\underset{H}{\overset{|}{\underset{|}{C}}}}-C\equiv C-H \qquad (2)$$

II

This differs from a double tautomerization in that it is not spontaneous. If the 1-alkyne is heated with alcoholic potassium hydroxide, isomerization takes place in the reverse direction, whereby 1-alkynes produce 2-alkynes. For the present purpose, the 2-alkyne is isomerized to the 1-alkyne as in (2). Observe that the resulting 1-alkyne, II, has one more CH_2 group in the chain than the starting 1-alkyne, I. If II is converted to its sodium alkynide and methylated with methyl bromide as in (1), when the product is isomerized to a 1-alkyne, the next higher homolog of II results.

$$R-CH_2-C\equiv C-H \xrightarrow{NaNH_2} R-CH_2C\equiv CNa \xrightarrow{CH_3Br}$$

$$R-CH_2C\equiv C-CH_3 \xrightarrow[\Delta]{NaNH_2\ cat.} R-CH_2-CH_2-C\equiv C-H$$

Thus, a 1-alkyne may be converted to its next higher homolog.

The ability of 1-alkynes to form metal salts makes it possible to separate or distinguish them from other hydrocarbons such as alkanes, alkenes, and disubstituted acetylenes. Among the hydrocarbons, only a 1-alkyne, R—C≡C—H, will form a precipitate with an ammoniacal cuprous salt, so that this reaction provides qualitative evidence for the presence of a 1-alkyne. The reaction may also be used to separate a 1-alkyne from a mixture containing other classes of hydrocarbons, or even to remove impurities of 1-alkynes from the other hydrocarbons. The alkynes are regenerated from the cuprous salts by treatment with dilute mineral acid.

4.4 USES OF ACETYLENE

Acetylene, mixed with air within a 5–80 per cent range, will explode violently when ignited. The flame of acetylene burning in oxygen is extremely hot, about 4000°, and therefore oxyacetylene torches are used for cutting and welding steel. Twenty per cent of the acetylene produced is used for this purpose; the other 80 per cent is used for producing chemicals. Most of the organic-chemical industry of Germany during the war years stemmed from acetylene, thanks to the work of a German chemist, J. Walter Reppe, and his co-workers. Previously acetylene under high pressure could not be handled safely; it frequently exploded for no apparent reason. Reppe bravely developed techniques of handling acetylene under high pressure for producing several low-molecular-weight chemicals. He also worked out new types of reactions which opened up a new field of chemistry. One of the most important products to come out of Reppe's work was polyvinylpyrrolidone (PVP) (page 555), which was used as a plasma extender in the treatment of hundreds of thousands of German casualties of World War II. PVP is used extensively now as the basic film-forming ingredient in 75 per cent of all hair preparations.

The major routes from acetylene to the many chemicals produced are indicated on the chart shown in Figure 4.4.

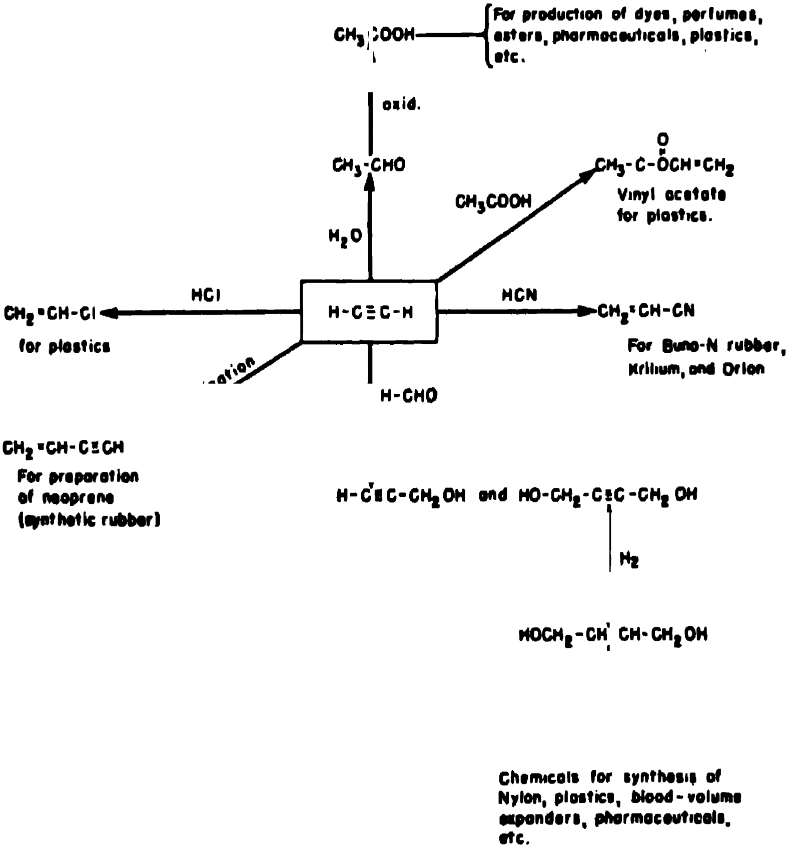
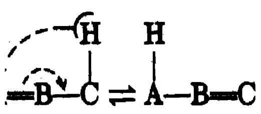

CH3COOH
For production of dyes, perfumes, esters, pharmaceuticals, plastics, etc.
oxid.
CH3-CHO
H2O
CH3COOH
CH3-C(=O)-OCH=CH2
Vinyl acetate for plastics.
HCl
CH2=CH-Cl
for plastics
H-C≡C-H
HCN
CH2=CH-CN
For Buna-N rubber, Krilium, and Orion
..ation
H-CHO
CH2=CH-C≡CH
For preparation of neoprene (synthetic rubber)
H-C≡C-CH2OH and HO-CH2-C≡C-CH2OH
H2
HOCH2-CH=CH-CH2OH
Chemicals for synthesis of Nylon, plastics, blood-volume expanders, pharmaceuticals, etc.

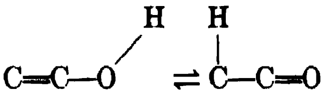
Fig. 4.4. Major routes from acetylene to various chemicals.

4.5 TAUTOMERISM

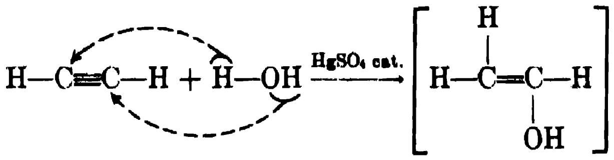
Another phenomenon which is unique among organic compounds is *tautomerism*. It is an isomerization in which a proton migrates in one direction and a covalent bond in the opposite direction within a molecule. Whenever three atoms, A, B, and C, are arranged so that there is a multiple bond between two and a hydrogen atom on the third, this special isomerization may occur.



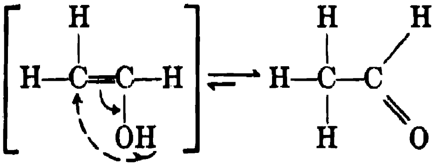
It is a reversible reaction, the position of equilibrium depending upon the nature of atoms A, B, and C. The most common situation is one in which two atoms are carbon and the third is oxygen, giving the structures of an enol (α-hydroxy-alkene) and a carbonyl compound:



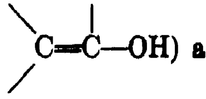
Such a molecular rearrangement occurs in the hydration of acetylene in acid solution in the presence of mercury salts.



The expected product is vinyl alcohol, $CH_2{=}CHOH$; but instead, the isolated product is acetaldehyde, $CH_3{-}CH{=}O$. This is due to the tautomerization of vinyl alcohol.



The equilibrium lies over 99 per cent on the right; not even detectable amounts of vinyl alcohol are present. That is why brackets are used around the vinyl alcohol formula.

This tautomeric system between an enol (combination of *en* for C=C and -ol for alcohol, having a structure  $>C{=}C(-)-OH$) and a carbonyl compound will be encountered several times in the book. In some cases the equilibrium will lie far on the enol side, other times far on the keto side, and at other times it will lie between the two extremes. However, tautomerism occurs among other couples (see page 428) and is a special form of isomerization. It is an isomerization which does not require a catalyst, although it may be catalyzed by certain reagents. The two isomers in equilibrium are called *tautomers* and the process of going from one tautomer to the other is called *tautomerization.*

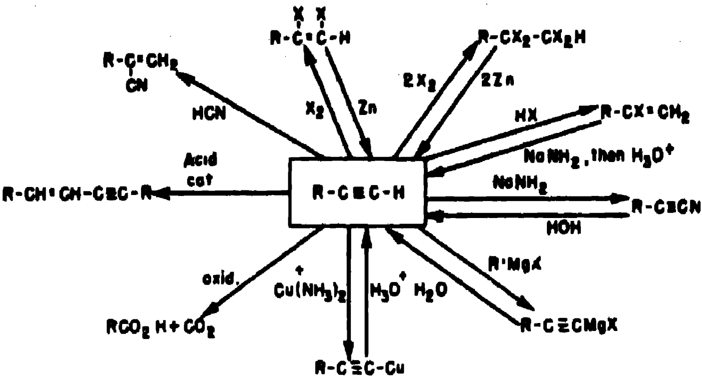


Fig. 4.5. Characteristic reaction chart for alkynes.

STUDY EXERCISES

1. Give equations for two general laboratory methods of preparing alkynes.

2. Starting with calcium carbide, how can the following be prepared: (a) dibromoethylene, (b) ethylene bromide, (c) 1,1-dibromoethane, (d) bromoethylene, (e) vinylacetylene, (f) cuprous acetylide, (g) *sym*-tetrabromoethane? Which of these compounds may be converted into acetylene? How?

3. How is acetylene produced industrially?

4. A sample of pure hydrocarbon when treated with a solution of bromine in CCl_4 quickly decolorized it without the evolution of HBr. What was signified by this test?

5. To what classes of hydrocarbons may the following belong? (a) $C_{16}H_{28}$, (b) C_6H_{14}, (c) $C_{18}H_{36}$, (d) $C_{11}H_{22}$.

6. By means of equations, show how the following syntheses may be brought about in the laboratory: (a) methylacetylene from acetylene, (b) 1-butyne from acetylene, (c) 2-pentyne from 1-pentyne, (d) 1,3-butadiene from 2-butene, (e) propyne from propene, (f) pentachloroethane from acetylene.

7. What are commercial sources of low-molecular-weight alkanes, alkenes, and acetylene?

8. Indicate the reagent or reagents that would be used for carrying out the following changes in the laboratory in one reaction vessel:

(a) $CH_3—CH_2—C≡C—H \rightarrow CH_3—CH_2—C≡CNa$

(b) $CH_3—CH_2—C≡C—H \rightarrow CH_3—C≡C—CH_3$

(c) $(CH_3)_2CH—C≡C—H \rightarrow (CH_3)_2CH—C≡C—Cu$

TEST QUESTIONS, Set 4

1. List the following in order of increasing acidity: methylacetylene, water, acetic acid, propene.

2. What volume of acetylene, STP, could be made from 40 g of calcium carbide which is only 90% pure?

3. How might one remove impurities of (a) ethylene and acetylene in ethane and (b) propyne in propene?

4. Given a sample of a clear, colorless liquid known to be either *n*-hexane, 1-hexene, or 1-hexyne, how would one proceed to determine which it is by qualitative test-tube experiments?

5. If 39.2 g of 1,1,2,2-tetrachlorobutane were heated with excess zinc dust and the product bubbled through an ammoniacal cuprous chloride solution, what weight of precipitate would be formed if the over-all yield were 70%?

6. How could one label bottles containing the isomers 2-butyne and 1,3-butadiene by using qualitative test-tube experiments?

7. What series of laboratory reactions could be used to convert (a) isopropyl alcohol to propyne, (b) 1-butene to 2-butyne, (c) *n*-pentyl bromide to 1-pentyne, (d) 4-methyl-2-hexyne to 2,3-dimethylhexane?

8. A compound A, C_5H_8, reacts with ammoniacal silver nitrate to form a precipitate. Oxidation of A with excess $KMnO_4$ yields an acid of the structure, $CH_3—CH(CH_3)—COOH$. What is the structural formula of A?

9. Since carbon uses *sp* hybrid orbitals in HCN, is the HCN molecule linear or angular?

10. Given three unlabeled bottles A, B, and C, each containing a colorless liquid. The liquid in A is inert to aqueous $KMnO_4$, and it is identical to the compound produced by the reduction of neopentyl chloride with HI and phosphorus. The liquid in B is found to have a molecular formula of C_6H_{10}, adds two moles of bromine per mole of C_6H_{10}, and produces $CH_3—CHBr—CH{=}CH—CHOH—CH_3$ upon the addition of HOBr. The liquid in C also has a molecular formula of C_6H_{10}, is inert to ammoniacal silver nitrate, and upon hydration in sulfuric acid produces $CH_3—CH_2—CO—CH_2—CH_2—CH_3$.

How would you label the bottles? Show how you reached your answer.

11. When propyne is hydrated in sulfuric acid, $CH_3—CO—CH_3$ is obtained rather than $CH_3—CH_2—CHO$. What does this show regarding the direction of addition of water to propyne?

5

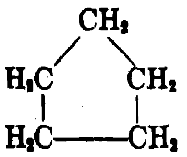
Alicyclic Hydrocarbons

Up to now we have dealt with compounds in which the carbon backbones have formed open chains with various degrees of branching. These are classified as aliphatics. Now we will consider compounds in which the carbon framework consists of rings, classified as *carbocyclics*. There are two types of carbocyclic compounds; those with properties resembling the aliphatics, called *alicyclics*, and those that are unsaturated but do not have olefinic properties, called *aromatics*. Aromatics will be discussed in Chapter 7.

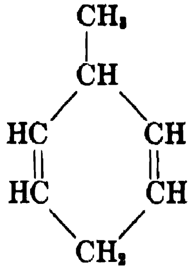
The isolation of compounds with other than six carbon atoms in a ring came rather late in the early history of organic chemistry, but now rings of four to eight carbon atoms are found in petroleum, and others have been synthesized with more than 30 carbon atoms in a ring. Many of the large ring compounds have odors of natural musk, cedar, etc., and are used in perfumes.

5.1 NOMENCLATURE

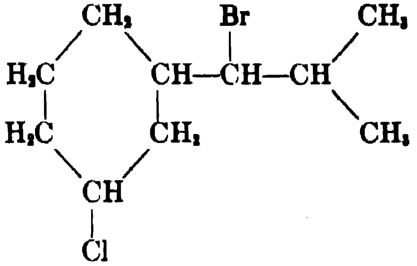
The cycloalkanes may be thought of as the products of joining open-chain alkanes together by the end carbon atoms through the loss of two hydrogen atoms. Their family empirical formula therefore has two less H's than the alkanes, giving C_nH_{2n}. The cycloalkenes have the formula C_nH_{2n-2} which is the same as that for open-chain alkynes. Thus, each loss of two H's from the empirical formula of the alkanes, C_nH_{2n+2}, indicates the presence of an additional bond between two carbon atoms, either another multiple bond or an additional ring. The saturated alicyclic hydrocarbons, cycloparaffins, are also called *naphthenes* in the petroleum industry because some of them have been isolated from the *naphtha* fraction of petroleum. Naphthas are cuts overlapping the ligroin and gasoline fractions of petroleum and are used as solvents. In naming the alicyclics, one merely uses the system used for the aliphatics and adds the prefix *cyclo*. Thus, the body of the name denotes the number of carbon atoms in the ring, the suffix indicates the class, the prefix shows what substituents are present and where, and positions in the side chain are denoted by the Greek alphabet. Several examples will serve as illustrations. The carbon atoms may be numbered clockwise or counterclockwise, and by convention one usually starts at the carbon atom which determines the class.



Cyclopentane

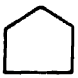


3-Methyl-1,4-cyclohexadiene

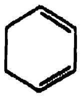


1-Chloro-3-(α-bromo-β-methylpropyl)-cyclohexane

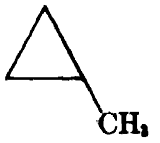
For convenience and simplicity, aliphatic rings are often represented by polygons, and it is understood that there is a CH_2 group at each corner unless some substituent is indicated. For example,



Cyclopentane



1,3-Cyclohexadiene



Methylcyclopropane

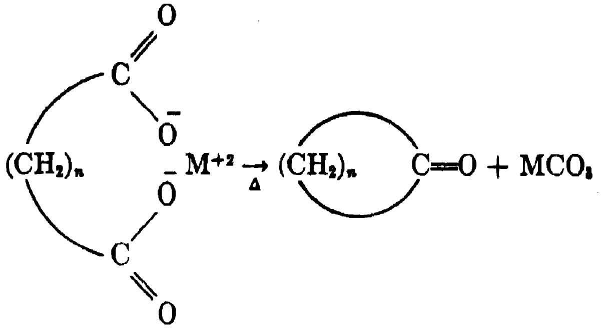
5.2 PREPARATION

There are many methods for forming alicyclic rings, but only a few of the most common procedures will be given. Alicyclics are grouped according to their ring sizes as follows:

Small	C_3 and C_4	Medium	C_8–C_{11}
Regular	C_5–C_7	Large	C_{12} and larger

Certain preparative methods are better than others for a given ring size and this factor must be considered in choosing a procedure for the preparation of an alicyclic.

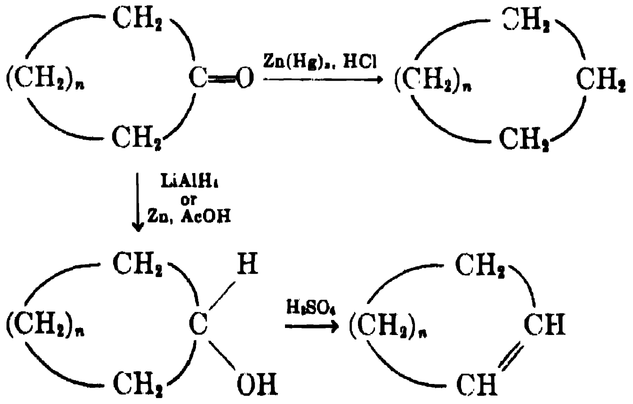
1. Prolysis of divalent metal salts of dicarboxylic acids[1]



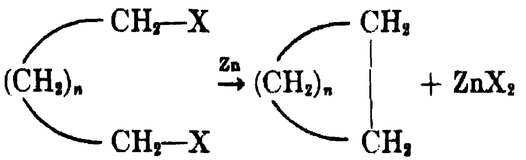
M = Ca, Th, Mn, etc.

A cycloalkanone
or
cyclanone

This reaction was the first used for the preparation of large rings although the yields were very low (0.1–8%). It can be used to prepare the regular ring-size compounds in reasonably good yields and should be restricted to this size ring. The cyclanones can readily be reduced to the corresponding cycloalkanes or cycloalkanols and the latter converted into cycloalkenes.



2. Freund reaction



$n = 1\text{–}4$

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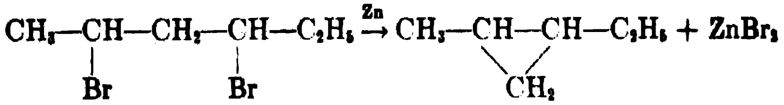
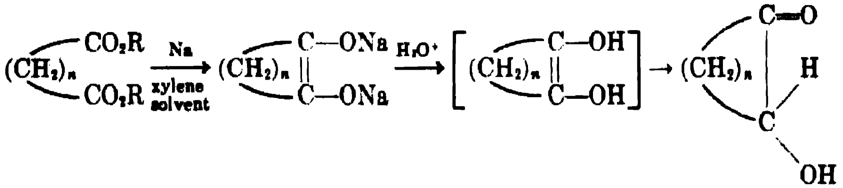
[1] L. Ruzicka, *et al.*, *Helv. Chim. Acta*, **9**, 499 (1926); **15**, 1459 (1932); Anhydrous KF has been found to be a catalyst for the conversion of adipic acids to the corresponding cyclopentanones in good yields. The generality of this reaction for other size rings has not been noted. L. Rand, *et al.*, *J. Org. Chem.*, **27**, 1034 (1962).

This method is one of the few that gives satisfactory yields for small ring compounds. The reaction is conveniently run at room temperature in formamide as a solvent. An example of its application is the following:

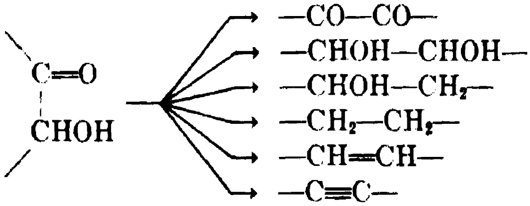


3. Acyloin condensation



$n > 6$

This method is applicable for rings of 8 or more carbon atoms and is the best method for the medium-size rings. The —CO—CHOH— grouping can easily be changed into several others by methods to be taken up later:



4. Use of carbenes

Carbenes are unstable fragments in which carbon has a pair of unshared electrons, RCH:. The simplest member is methylene, :CH_2, mentioned earlier (page 89). Very often the dihalocarbenes, :CX_2, are used because of their greater stability and end use of the products obtained. Carbenes are prepared by a variety of methods, but three common methods are the following:

Methylene

$$CH_2I_2 + Zn(Cu) \xrightarrow{\text{ether}} :CH_2 + ZnI_2\,.$$

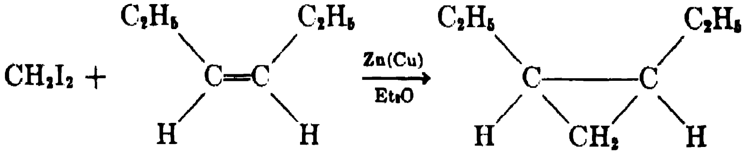
Alkylmethylene, RCH:

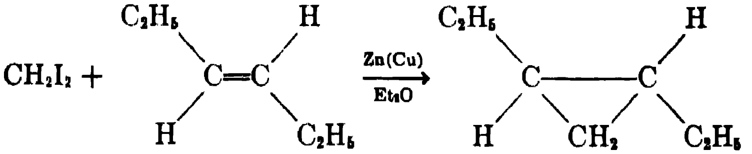
$$\underset{\substack{\text{An aliphatic}\\ \text{diazo compound}}}{RCHN_2} \xrightarrow{h\nu} RCH: + N_2$$

Dihalocarbene, $:CX_2$

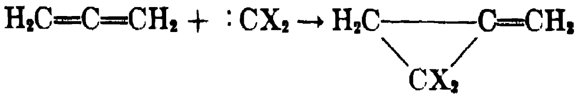
$$\left.\begin{array}{l} \quad HCX_3 \\ \text{or}\ \ X_3C—CO_2Na \\ \text{or}\ \ X_3C—COCX_3 \end{array}\right\} \xrightarrow[\text{heat}]{\text{base, or}} :CX_2$$

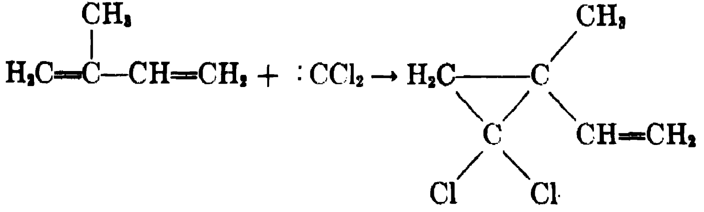
Carbenes are generally prepared in solution in the presence of the compound with which they are to react. Carbenes add *cis* to C=C bonds to produce substituted cyclopropanes: For illustration, *cis*-3-hexene gives pure *cis*-1,2-diethylcyclopropane and *trans*-3-hexene gives only the *trans*-1,2-diethylcyclopropane with $:CH_2$.





Furthermore, carbenes add almost exclusively 1,2 to a conjugated or cumulated diene system.





In selecting a method for the preparation of an alicyclic compound from an aliphatic compound among those given here, one would give consideration to ring size as follows:

	Method of Choice
Small rings	Freund reaction or use of carbenes
Regular size rings	Freund reaction or pyrolysis of salts (and Dieckmann condensation given later. Cf. page 379).
Medium size rings	Acyloin condensation
Large rings	Acyloin condensation

A few other methods will be added to this list later.

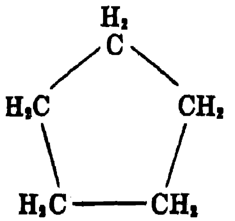
5.3 PHYSICAL AND CHEMICAL PROPERTIES

Although there is a trend of increasing melting and boiling points with rise in molecular weights of the alicyclic hydrocarbons, there is some fluctuation in values (see Table 5.1).

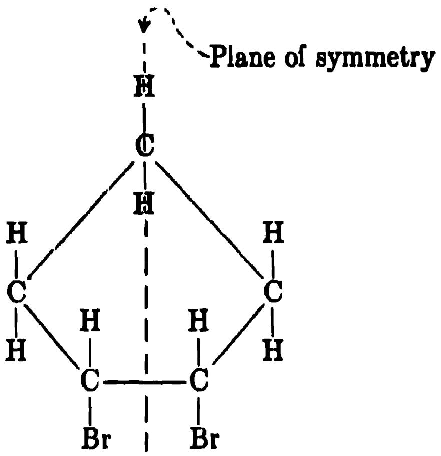
TABLE 5.1. PHYSICAL CONSTANTS OF SOME ALICYCLIC HYDROCARBONS

Name	Melting Point	Boiling Point	Sp. Gr. (liq.)
Cyclopropane	−127	−33	0.688
Cyclobutane	−80	13	.704
Cyclopentane	−94	49	.746
Cyclohexane	6.5	81	.778
Cycloheptane	−12	118	.810
Cyclooctane	14	149	.830
Methylcyclopentane	−142	72	.749
Methylcyclohexane	−126	100	.769
Cyclopentene	−93	46	.774
Cyclohexene	−104	83	.810
1,3-Cyclopentadiene	−85	42	.798
1,3-Cyclohexadiene	−98	81	.840
1,4-Cyclohexadiene	−49	87	.847

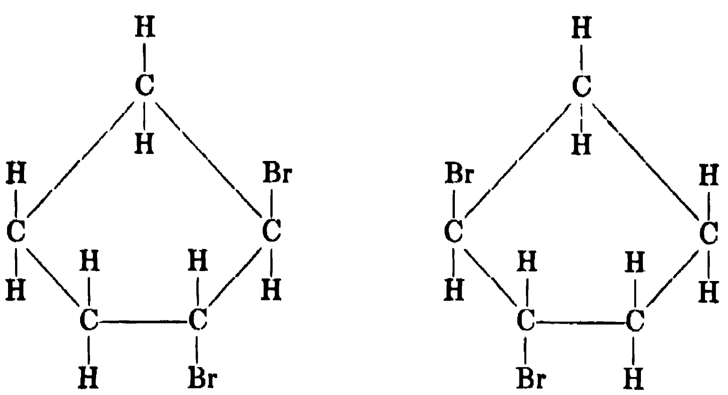
The chemical properties of alicyclics are quite similar to those of aliphatics, although the presence of a ring will make certain differences. For example, cycloalkanes, like alkanes, are inert to oxidizing and reducing agents, ozone, and acids and bases, but are smoothly halogenated. The ring geometry, however, gives the cycloalkanes a symmetry which makes all the hydrogen atoms equivalent. Accordingly, each cycloalkane gives rise to only one monobromination or monochlorination product, whereas an alkane will produce several. Thus, there are three bromo-*n*-pentanes but only one bromocyclopentane. Irrespective of which hydrogen atom in cyclopentane is replaced, the product is the same, for each product fits the same mold and merely differs in its orientation in space from the others. E.g.



On the other hand, when a second substitution is made, a hydrogen may be placed on the already substituted carbon or on the C_2 or C_3 carbon atom of the cyclopentane ring. Thus, there can be 1,1-, 1,2-, or 1,3-dibromocyclopentane. Furthermore, if one of the latter position-isomers is produced, the two bromine atoms may be on the same side of the ring or on opposite sides. The isomer with the two substituents on the same side is a *cis* isomer and that with substituents on opposite sides of the ring is a *trans* isomer. Hence, there is the *cis*-1,2-dibromocyclopentane and the *trans*-1,2-dibromocyclopentane. These are geometric isomers, and both are position isomers of the 1,1-dibromocyclopentane. Furthermore, there is no plane of symmetry in the *trans*-1,2-dibromocyclopentane. It will be recalled from Section 1.6 that, as a general rule, when there is no plane of symmetry in a molecule, two such molecules will exist which are mirror images of each other. Thus, there is a dextrorotatory and a levorotatory *trans*-1,2-dibromocyclopentane.

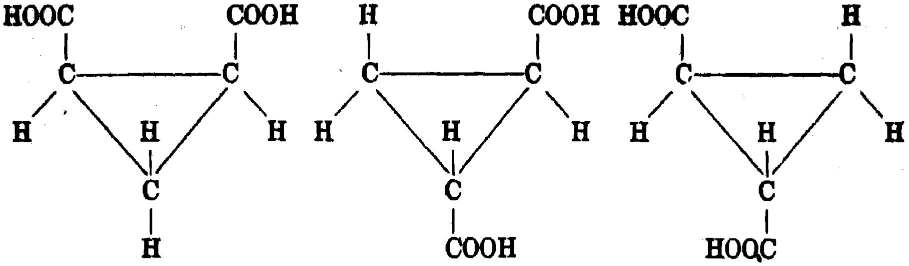


cis-1,2-Dibromocyclopentane



Nonsuperposable mirror images of *trans*-1,2-dibromocyclopentane

Racemic *dl-trans*-1,2-dibromocyclopentane is very difficult to resolve, but *dl-trans*-cyclopropane-1,2-dicarboxylic acid has been resolved, as well as many other asymmetric alicyclic racemates.

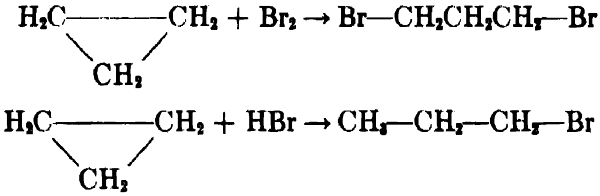


cis-Cyclopropane-1,2-dicarboxylic acid
m.p. 139°

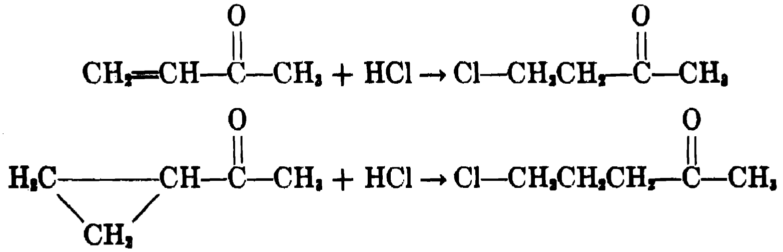
d- and *l*-forms of *trans*-cyclopropane-1,2-dicarboxylic acid
dl-acid; m.p. 175°
d-acid, m.p. 175°; *l*-acid, m.p. 175°
$[\alpha]_D = \pm 84.4°$

Another property exhibited by alicyclic compounds attributable to the presence of the ring structure is *ring-strain*. There are three types, commonly referred to as *bond-angle* or *Baeyer strain*, *Pitzer strain*, and *transannular strain*. For illustration, cyclopropyl groups resemble ethylenic groups to a certain extent in that both types undergo addition reactions.

$$CH_2{=}CH_2 + Br_2 \rightarrow Br{-}CH_2{-}CH_2{-}Br$$

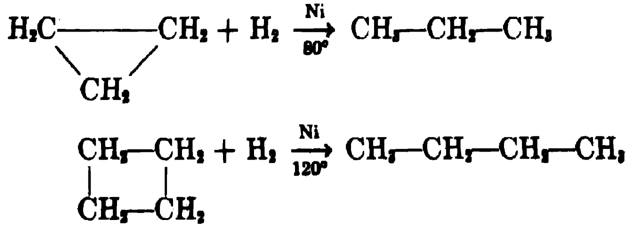


and



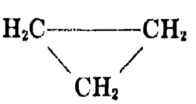
$$CH_2{=}CH{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}CH_3 + HCl \rightarrow Cl{-}CH_2CH_2{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}CH_3$$

Cyclopropane and cyclobutane also add hydrogen, although cyclobutane

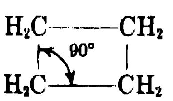


requires a higher temperature. The higher cycloalkanes do not undergo addition reactions and are inert to hydrogen at temperatures below that where thermal cracking begins. To explain this olefinic character of cyclopropane and its derivatives, Baeyer[3] proposed in 1885 the idea, that since cyclopropane is an equilateral triangle, the carbon bonds form angles at 60°. Normally, the four valences of carbon point toward the corners of a tetrahedron, forming interbond angles of 109°28′, or approximately 110°. Hence, each carbon bond in cyclopropane is bent inward $\frac{110 - 60}{2} = 25°$ from its normal bond angle. This creates a bond strain within the molecule, and the molecule tends to relieve this strain by opening the ring through addition reactions. Baeyer computed the angles of distortion for ethylene and cyclopropane to cyclohexane as follows:

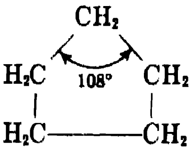
$$CH_2{=}CH_2 \; : \; \frac{110 - 0}{2} = 55° \text{ inward}$$



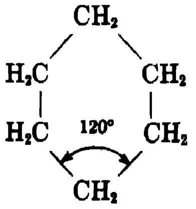
$$: \; \frac{110 - 60}{2} = 25° \text{ inward}$$



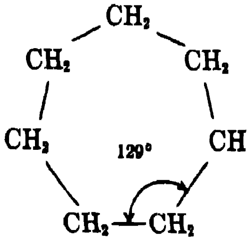
$$: \; \frac{110 - 90}{2} = 10° \text{ inward}$$



$$: \; \frac{110 - 108}{2} = 1° \text{ inward}$$



$$: \; \frac{120 - 110}{2} = 5° \text{ outward}$$



$$: \; \frac{129 - 110}{2} = 9.5° \text{ outward}$$

It can be seen that alkenes have the greatest strain, which partially accounts for their high reactivity in addition reactions. Cyclopentane is virtually free of ring-strain. According to Baeyer's idea, cyclohexane should have a small

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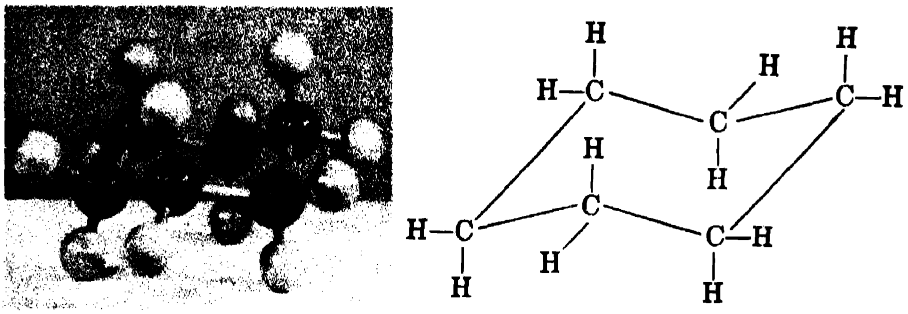
[3] Adolf von Baeyer, a German organic chemist, received the Nobel Award in chemistry in 1905.

ring-strain and cycloheptane should have as much strain as cyclobutane. Neither of these expectations is observed. Sachse (1890) offered an explanation for this discrepancy by suggesting that rings of five carbon atoms or fewer are essentially planar with respect to the carbon atoms, while those of six or more are puckered. Thus, cyclohexane has what is called a *chair conformation*.



Chair conformation of cyclohexane

Fig. 5.1.

It is found from thermochemistry that for a series of related compounds, the more stable the compound the smaller is its heat of combustion. On this basis, the instability of cycloalkanes relative to *n*-alkanes has been computed as given in Table 5.2.

TABLE 5.2. RING-STRAIN IN CYCLOALKANES

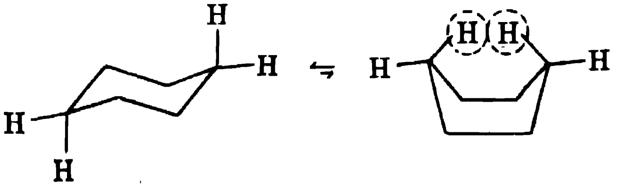
n in C_nH_{2n}	*Ring-strain*
3	27.6 kcal/mole
4	26.2
5	6.5
6	0
7	6.3
8	9.6
9	12.6
10	12.0
11	11.0
12	3.6
14	0
16	1.6

The ring-strain in cycloalkanes is shown in Table 5.2 to be very large for small rings, passes through a minimum with the normal-size rings, reaches a maximum with the medium-size rings, and falls off again to a low value for the large rings.

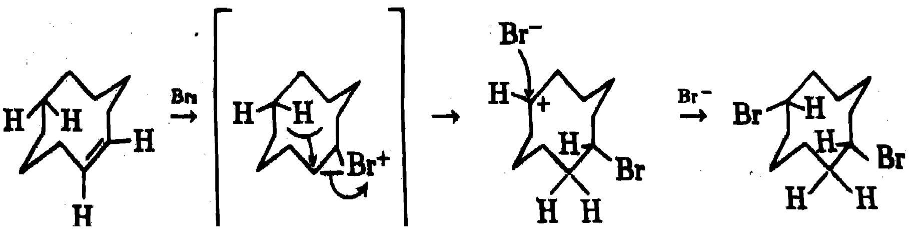
Baeyer's bond-angle strain proposal accounts for the large strain in the C_3

and C_4 rings, as well as for the olefinic character of cyclopropyl derivatives. His notion, however, does not explain the lack of strain in cyclohexane nor the much greater ring-strain of cyclobutane over that of cycloheptane. It is observed that cyclopentane has some ring-strain although it should have no bond-angle strain. Apparently there is some other type of strain in the molecule. Examination of a model of cyclopentane reveals that the five carbon atoms are planar and the hydrogen atoms are eclipsed across each C—C bond. Thus, there is a repulsion between the adjacent hydrogen atoms as there is in the eclipsed structure of ethane. This produces a certain strain relative to an open chain, where the CH_2 groups can have a staggered *trans conformation.* This type of strain is called *Pitzer strain.* Note from models that the CH_2 groups in the chair conformation of cyclohexane are staggered across each C—C bond. Thus, the molecule has no bond angle strain or Pitzer strain.

By a twist of the C_6 ring, the *chair* structure can be transformed into a *boat* structure.



This brings the hydrogen atoms on the bow and on the stern carbon atoms very close to each other. The ensuing repulsion makes the boat conformation unstable relative to the chair by about 6 kcal/mole and accounts for the fact that at ordinary temperatures cyclohexane exists entirely in the chair conformation. This strain due to repulsion between atoms across a ring (between atoms attached to ring atoms at least two carbon atoms apart) is called *transannular strain.* This is the type of strain found in the medium-size rings. Apparently these rings have conformations which bring certain atoms across the ring very close together and lead to many transannular reactions. For example, when bromine is added to cyclodecene, instead of getting the 1,2-addition product, one gets a 1,6-dibromocyclodecane.

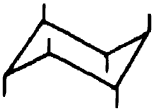


In summary, the principal types of strain in the cycloalkanes is as follows:

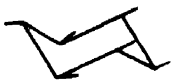
C_3, C_4	Bond-angle, some Pitzer.
C_5—C_7	Pitzer
C_8—C_{11}	Transannular, some Pitzer
$>C_{11}$	Pitzer

Because of bond angle strain, the C_8 ring is the smallest ring in which the C≡C bond has been found (recall that the —C≡C— link is linear), and the C_8 ring is the smallest ring in which a *trans* C=C bond has been observed.

One more aspect of the alicyclic rings to point out is that the rings larger than C_5 undergo various distortions and inversions. The cyclohexane ring has been studied the most. In the chair conformation there are C—H bonds of two types. Six parallel the axis as in I and are called *axial*

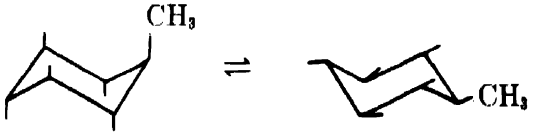


I



II

(symbolized *a*) and six radiate outward at angles of 109.5° to the axis as in II, and are called equatorial (symbolized *e*). The cyclohexane ring is quite flexible and one chair conformation III can invert into another chair conformation IV. All bonds which were axial in III are equatorial

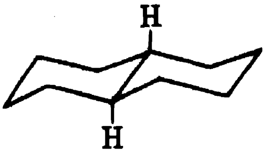


III IV

in IV, and those which were equatorial in III are axial in IV. The two forms are equivalent and indistinguishable when all atoms on carbon are identical.

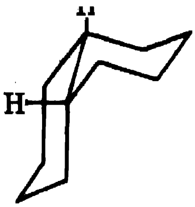
In a monosubstituted cyclohexane, the substituent may occupy an axial or an equatorial position. A study of scale models shows that the axial CH_3 in III is closer to the axial H's on the same side of the ring (1:3 diaxial repulsion) than the equatorial CH_3 is to the adjacent axial or equatorial H's (1,2-repulsion). As a result, conformer IV is more stable than III and, as a general rule, substituents preferably assume equatorial orientations.

So far, the discussion of alicyclics has been limited to single-ring compounds. Essentially the same conformational concepts considered already apply as well to polycyclic compounds. Decalin, for example, consists of two fused cyclohexyl rings in which each ring may assume a chair or boat configuration and the junction between rings may be *cis* or *trans*.



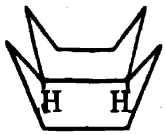
trans-Decalin

V



cis-Decalin

VI

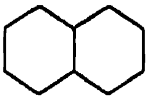


Boat-boat form of *cis*-decalin

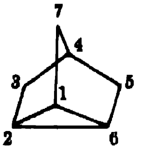
VII

Isomer VII is obviously the least stable because of the strain of two boat configurations of a cyclohexyl ring. Although either ring of the *trans* isomer could flip to a boat form, both rings cannot invert to the reverse chair forms as does cyclohexane. The student should use models to convince himself of this. Consequently, *trans*-decalin is a fairly rigid molecule.

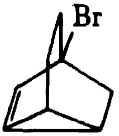
The fused-ring polycyclic compounds, i.e., those with two or more carbon atoms common to two or more rings, are named on a basis of the number of atoms in the carbon-framework, the number of rings involved, and the number of atoms in each bridge. Some examples are given below for illustration.



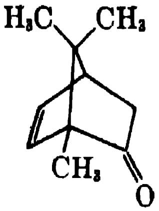
Bicyclo[4.4]decane
or
decalin



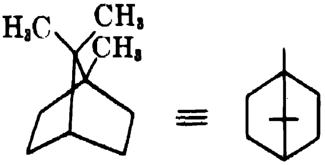
Tricyclo[2.2.$1^{2,6}$]heptane



1-Bromobicyclo[2.2.2]oct-2-ene

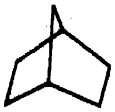


1,7,7-Trimethylbicyclo[2.2.1]hept-5-ene-2-one
or 5,6-dehydrocamphor

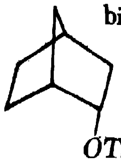


1,7,7-Trimethylbicyclo[2.2.1]heptane
or bornane

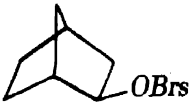
The prefixes *nor* and *homo* are used with the name of a parent compound to indicate one fewer or one more carbon atom, respectively, than in the parent compound. Actually, norbornane should be trisnorbornane, since it has three fewer carbon atoms than bornane, but for simplicity the tris has been dropped. The prefixes *endo* and *exo* refer to groups being on the same or opposite sides of a bridge, and *anti* and *syn* are used with groups on a bridge:



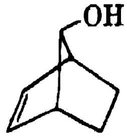
Norbornane or
bicyclo[2.2.1]heptane



Endo-norbornyl tosylate
(Ts = p-CH_3-C_6H_4-SO_2

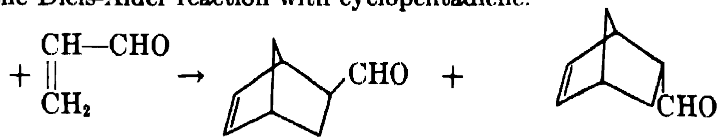


Exo-norbornyl brosylate
Brs = p-Br-C_6H_4-SO_2)



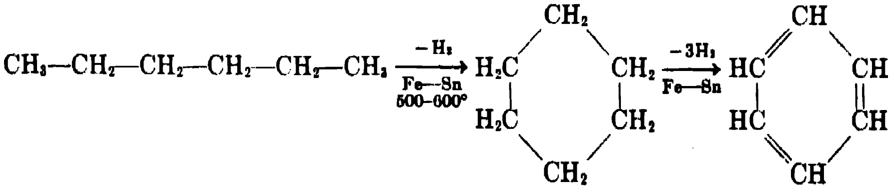
Anti-7-norborneol

A method often used for the preparation of some of these norbornene compounds is the Diels-Alder reaction with cyclopentadiene.



Other bicyclo and tricyclo compounds will be mentioned in the section on terpenes.

Unsaturated alicyclics may be hydrogenated as was described for alkenes, and they may be dehydrogenated. Again, the methods of dehydrogenation differ for laboratory and industrial scales. Commercially, dehydrogenation is carried out over catalysts made from chromium, silicon, iron, or other metals. This is a form of the aromatization process mentioned in Section 2.9f and discussed in Section 8.1, whereby aromatics are made from aliphatics.

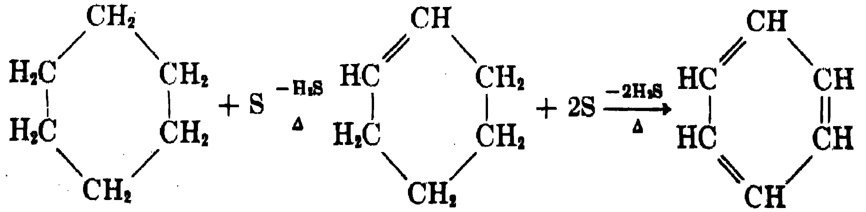


n-Hexane

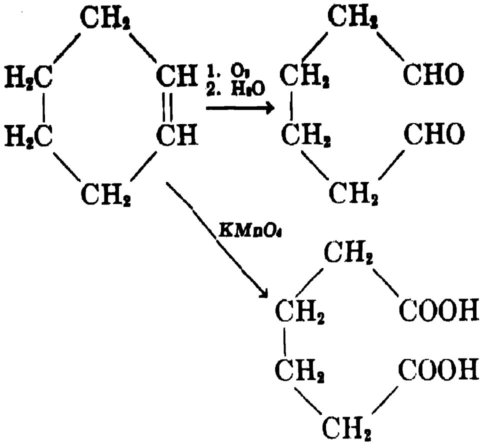
Cyclohexane

Benzene

In the laboratory, dehydrogenation may be accomplished by heating the alicyclic with selenium or sulfur.



Certain reactions of unsaturated alicyclics also reveal the presence of a ring structure. Ozonolysis of cyclohexene, for example, does not give two aldehyde molecules, but an open-chain molecule with two aldehyde groups. Similarly, its oxidation gives a single molecule with two carboxyl groups.

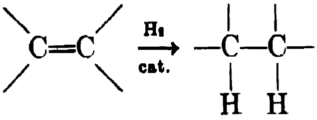


5.4 STEREOCHEMISTRY OF REACTIONS

The alicyclic compounds provide the best system for the elucidation of the stereospecificity of addition and elimination reactions. It is therefore appropriate to discuss the mechanisms of some of these reactions here.

Additions

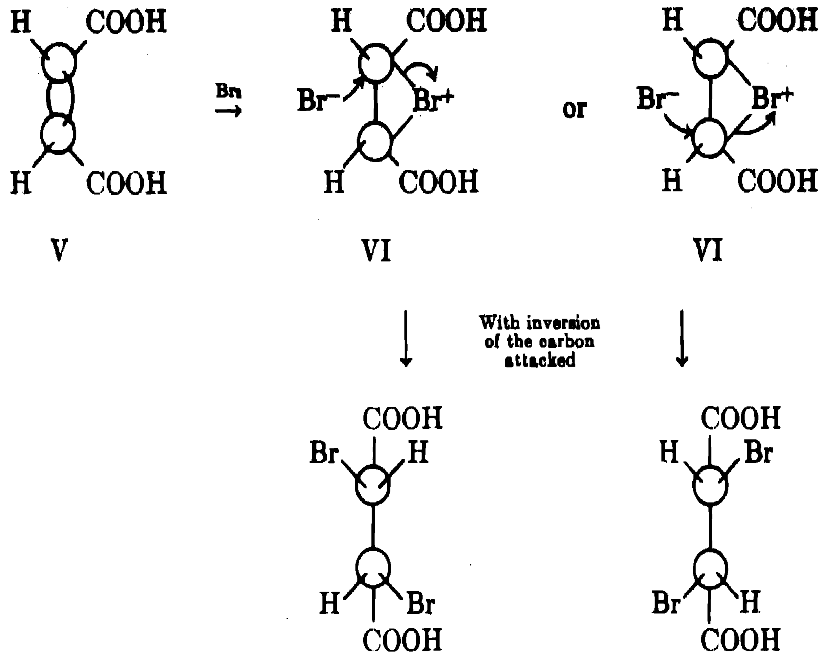
H_2



Catalytic hydrogenation goes by a *cis* addition, thus 2-butyne gives *cis*-2-butene. The most active catalysts are platinum, palladium, and Raney nickel, which can usually be used at low pressures and temperatures. Other metals such as copper, cobalt, or iron require high pressures and temperatures. The reactant sits on the surface of the catalyst and hydrogen approaches the C═C or C≡C bond from one side, possibly the catalyst side, with hydrogen dissolved in the catalyst. For this reason, the C═C bond must be able to get close to the surface of the catalyst and occasionally steric conditions about the C═C bond prevent this close proximity to the surface and hydrogenation cannot proceed.

X_2, HOX, HX

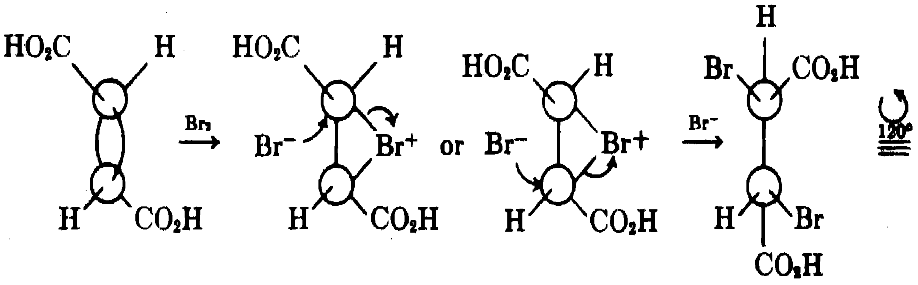
It was pointed out in Section 3.4a that these reagents add by a *trans*, polar mechanism. Thus, bromination of maleic acid (V) gives a racemic mixture of the dibromide (VII plus VIII) whereas fumaric acid gives the meso isomer (XII).



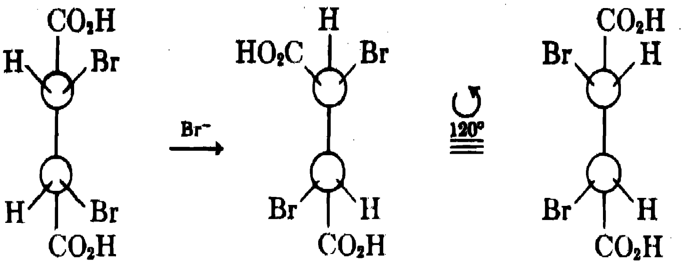
V VI VI

VII VIII

When bromine reacts with the alkene V to produce the intermediate or transition state VI, then Br⁻ ion approaches from the rear and may attack either carbon atom. The attacked carbon atom undergoes a Walden inversion whereby reaction with the top carbon yields VII and reaction with the bottom carbon atom yields VIII. VII and VIII are mirror images and therefore there results a racemic mixture. A similar reaction with fumaric acid yields only one product.



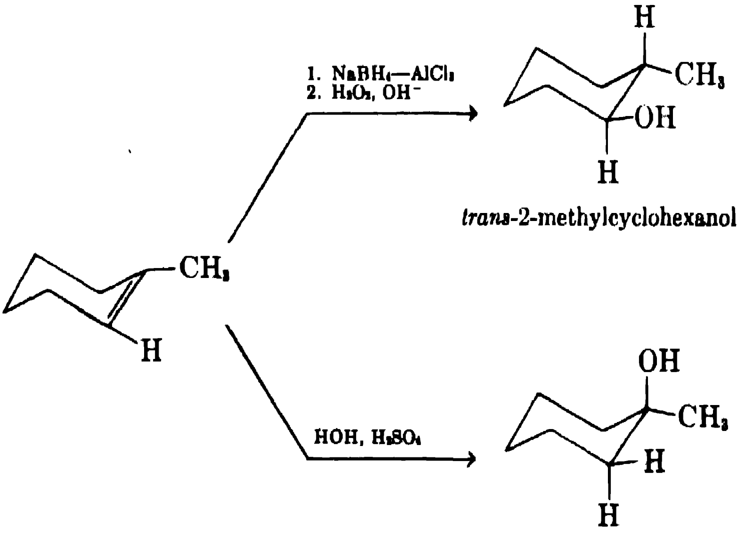
IX X X XI



XII XIII XIV

Rotation of the top group in XI through 120° produces XII, and rotation of the top group of XIII produces XIV. XII and XIV are the same molecule; XIV results when XII is turned upside down.

Hydration in sulfuric acid also goes by a *trans* addition but hydration through the hydroboration process takes place *cis* and toward the less hindered side. For example,

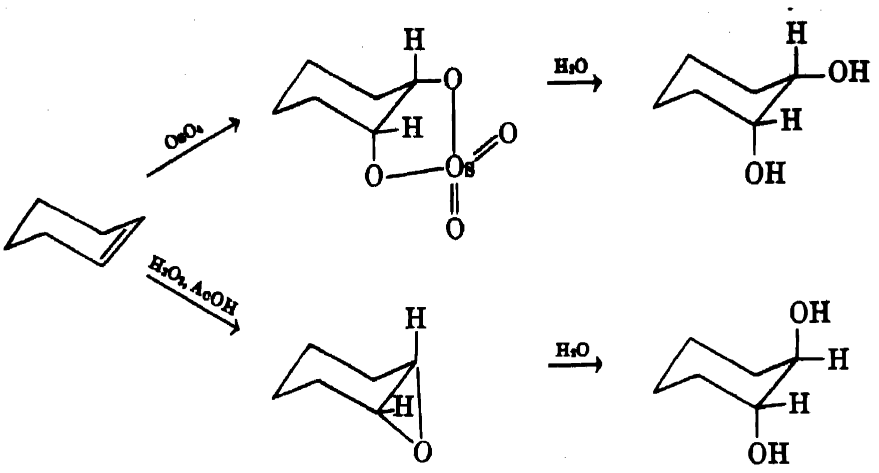


trans-2-methylcyclohexanol

1-Methylcyclohexanol

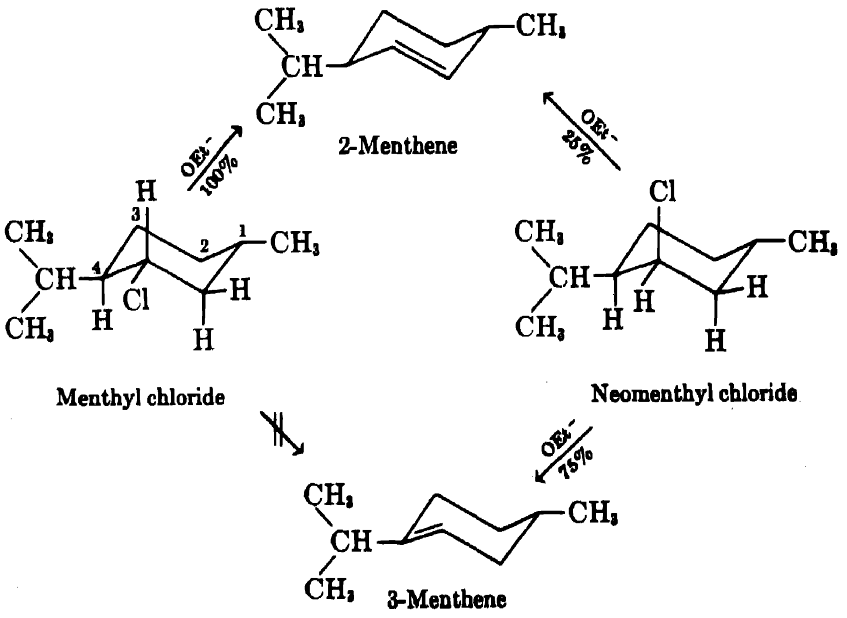
Hydroxylation (addition of two OH groups)

H_2O_2 in acetic or formic acid gives a *trans*-glycol, whereas osmium tetroxide gives a *cis*-glycol.



Eliminations

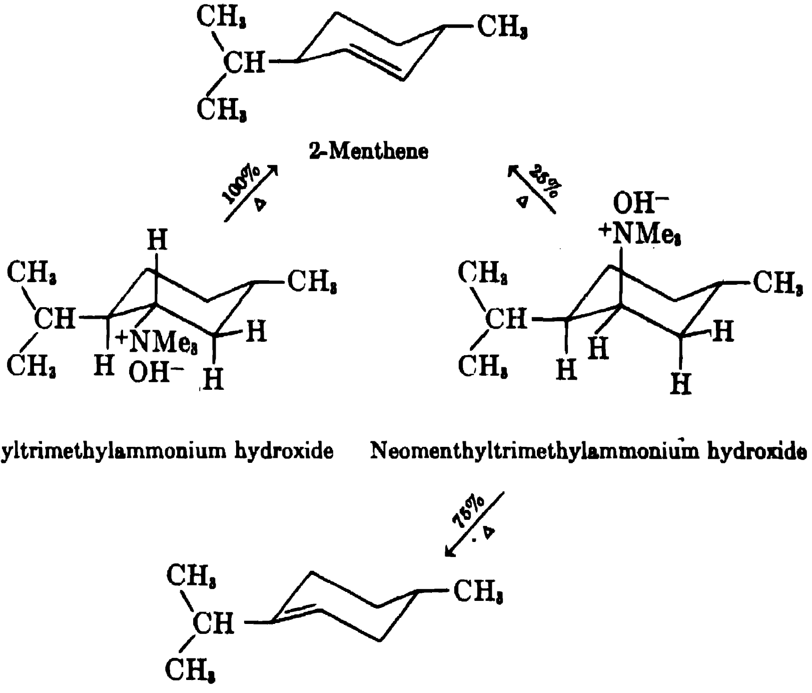
Dehydrohalogenation and dehydration take place by a *trans* polar stepwise or concerted mechanism. This was described in Section 3.2a, and the stereospecific course of the reaction can be illustrated by the dehydrohalogenation of menthyl and neomenthyl chlorides.



Menthyl chloride does not give any 3-methene because there is no H on

C_4 *trans* to the Cl atom on menthyl chloride. Neomenthyl chloride does, and can thereby give either isomer.

Pyrolytic decomposition of quaternary ammonium salts proceeds by a *trans* elimination (base catalysis leads to *cis* elimination).



2-Menthene

Menthyltrimethylammonium hydroxide

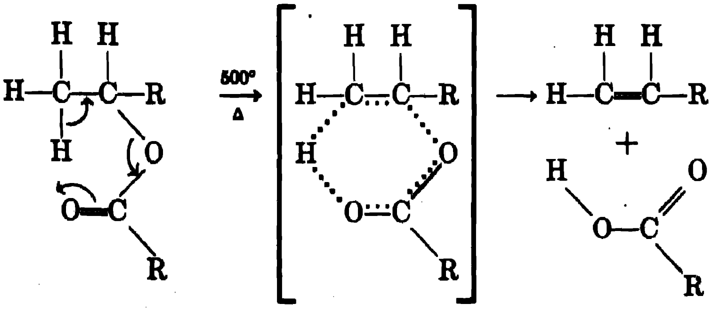
Neomenthyltrimethylammonium hydroxide

3-Menthene

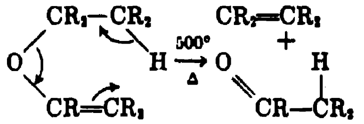
Again, the menthyl salt produces only the 2-menthene, whereas the neomenthyl salt, which has C_3—H and C_4—H bonds *trans* to the ammonium group, gives some of both isomers.

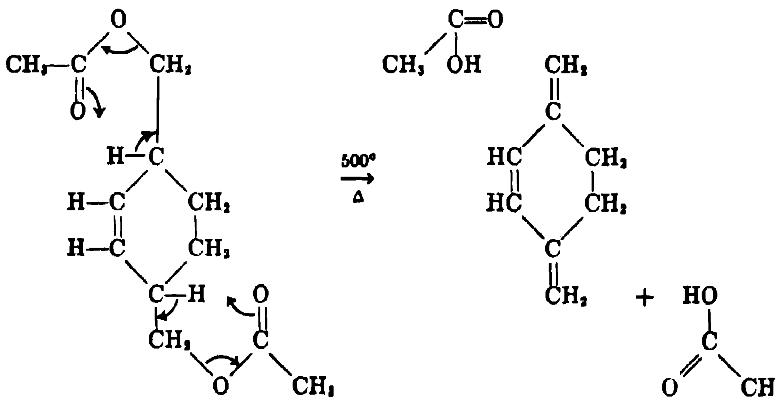
Pyrolysis of esters

In the rigid absence of any catalyst, esters of a carboxylic acid undergo a concerted *cis* elimination when heated to elevated temperatures.



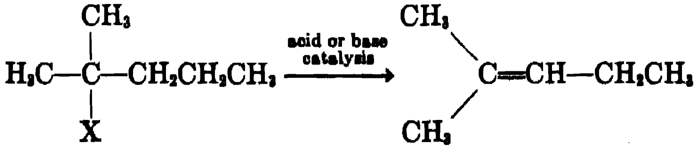
The arrows in the ester account for the final positions of the electrons and are not intended to mean that the electron-shift must be in the direction shown. Arrows in the opposite direction would also be valid. Various systems undergo such eliminations.





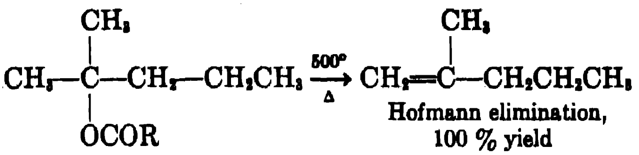
This is the only known way to prepare this conjugated triene, which is an isomer of *p*-xylene (p. 212). All other elimination methods of producing this system catalyze its isomerization to the more stable *p*-xylene, which is the only product. This shows that heat alone up to about 550° is really not a drastic condition, for this highly sensitive unsaturated compound can be produced under these conditions. Cold, concentrated sulfuric acid is far more severe, in which the hydrocarbon would rapidly react to give other substances. At higher temperatures, free radical random cracking sets in and a number of products are formed.

Not only the *cis* or *trans* course of addition and elimination reactions is of concern but also the question of which adjacent carbon atom will add or lose the proton. As a generality, additions are in accordance with Markownikoff's rule and eliminations follow Saytzeff's rule. However, hydration via the hydroboration reaction goes anti-Markownikoff, and anti-Saytzeff eliminations (called Hofmann eliminations) occur (1) with ester pyrolysis, (2) with onium compounds, and (3) when groups in the olefin would be spatially crowded (steric hindrance). For example,

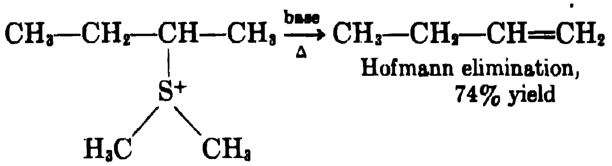


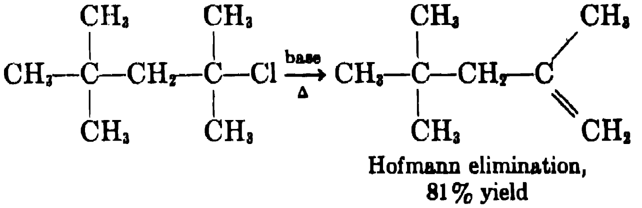
$$H_3C-\underset{X}{\overset{CH_3}{C}}-CH_2CH_2CH_3 \xrightarrow[\text{catalysis}]{\text{acid or base}} (CH_3)_2C{=}CH-CH_2CH_3$$

Saytzeff elimination, 75% yield

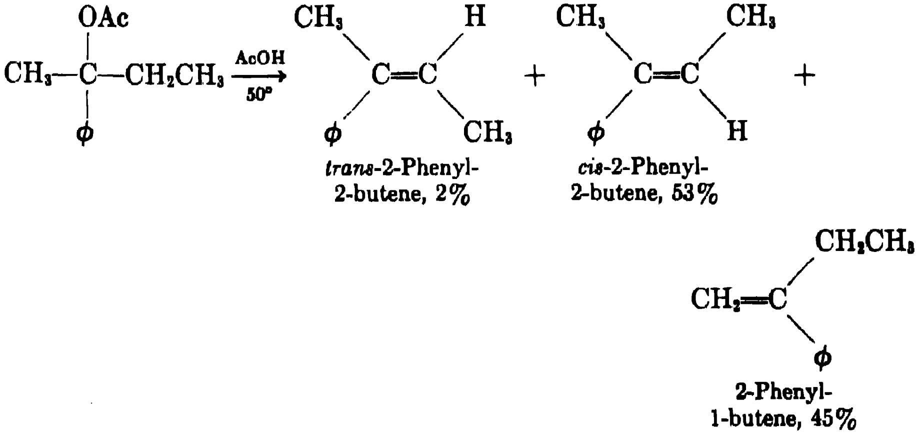


$$CH_3-\underset{OCOR}{\overset{CH_3}{C}}-CH_2-CH_2CH_3 \xrightarrow[\Delta]{500^\circ} CH_2=\overset{CH_3}{C}-CH_2CH_2CH_3$$

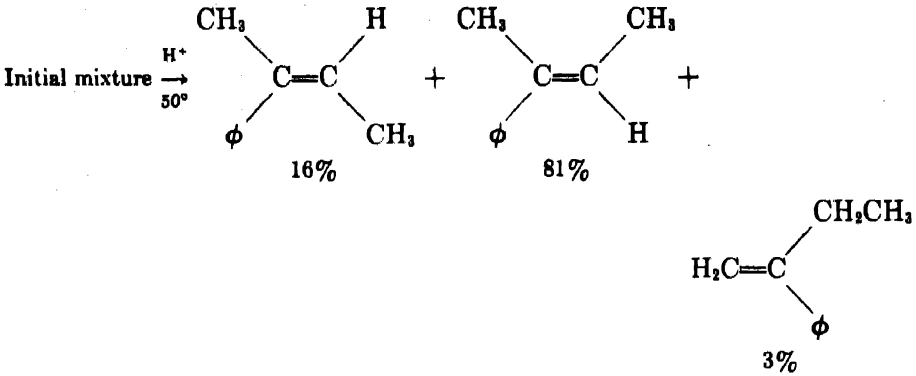




The stereochemical course of a reaction is influenced some by experimental conditions. We have seen that two or more products can be produced in most organic reactions. In some cases, the major product is the one produced by the fastest reaction, and in other instances, the most stable product is the principal product. The former case is said to be *kinetically controlled* and the latter is *thermodynamically controlled*. For example, when 2-phenyl-2-butyl acetate is heated in acetic acid at 50° in the absence of any added catalyst, an elimination reaction occurs to produce three products:



If then a trace of strong acid is added to the mixture of alkenes, the alkenes are converted to the equilibrium mixture in which most of the 1-butene is changed into 2-butene and the more stable *cis* isomer predominates.



Thus, the kinetically controlled product-mixture is converted into the thermodynamically controlled product-mixture. The latter mixture is also obtained if the original elimination is carried out in the presence of strong acid. Other examples of kinetically controlled products vs. thermodynamically controlled products are mentioned on pages 217 and 542.

This chapter has presented some of the basic chemical and physical properties of the alicyclic hydrocarbons and their simple derivatives. Their properties are of special interest for application to certain types of natural substances such as the steroids (e.g., cholesterol), the terpenes (e.g., camphor), and the alkaloids (e.g., strychnine, nicotine, morphine, etc.). Some of the chemistry of these more complex substances will be discussed in later chapters of this book.

STUDY EXERCISES

1. Give general equations for two methods of preparing cyclopropyl derivatives, two for preparing normal ring-size alicyclics, and one method for preparing medium-size and large ring compounds from aliphatic compounds.

2. Starting with 1,6-dibromohexane or $HO_2C—(CH_2)_7—COOH$, what series of reactions would you use in the laboratory to prepare (a) chlorocyclohexane; (b) 1,3-cyclohexadiene; (c) 1,2-dibromocyclohexane?

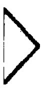
3. Write the structural formula for *cis*-3-methyl-4-bromocyclohexane.

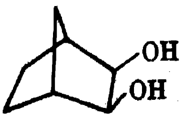
4. Write structural formulas for all possible isomers of 1,3-bromochlorocyclohexane.

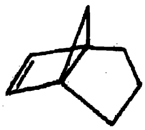
5. On the basis of the information given, how many rings does each of the following compounds contain:

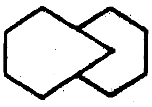
   (a) a terpene, $C_{10}H_{18}$, takes up no hydrogen;
   (b) a terpene, $C_{10}H_{16}$, reacts with bromine to form $C_{10}H_{16}Br_4$;
   (c) a steroid hydrocarbon, $C_{27}H_{48}$, does not add hydrogen;
   (d) a hydrocarbon, $C_{14}H_{10}$, adds hydrogen to form $C_{14}H_{24}$;
   (e) a hydrocarbon, $C_{18}H_{12}$, absorbs hydrogen to form $C_{18}H_{30}$.

6. Name the following compounds:

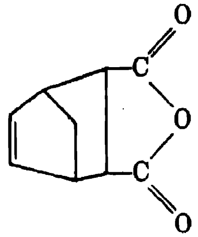








7. Propose a synthesis of the compound



8. Account for the fact that *trans*-decalin is more stable than the *cis* isomer.

9. Acetylene and ethylene react with cyclopentadiene in a Diels-Alder reaction under pressure and at elevated temperatures. Propose structures for the two products.

10. Suggest a route for the synthesis of 1,1-dimethyl-2,2-dibromocyclopropane.

TEST QUESTIONS, Set 5

1. What straight-chain compound would result from vigorous oxidation of cyclohexanol? Of what practical use is this reaction to the plastic industry?

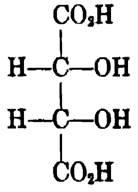
2. Would either *cis*- or *trans*-cyclohexane-1,4-dicarboxylic acid be asymmetric?

3. Which of the following are asymmetric:

trans-1,4-dibromocyclohexane
trans-1,3-dibromocyclohexane
cis-1,3-dibromocyclohexane
trans-1-bromo-4-chlorocyclohexane
cis-1-bromo-4-chlorocyclohexane

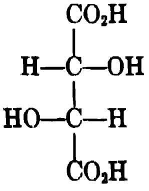
4. A compound of formula C_5H_{10} is known to be 2-pentene, cyclopentane, or 1,2-dimethylcyclopropane. How could one determine, by qualitative test-tube experiments, which of the compounds it is?

5. An oxidation of maleic acid gave meso-tartaric acid, whereas a similar oxidation of fumaric acid gave a racemic mixture of *d*- and *l*-tartaric acids. Offer an explanation for the type of products obtained.



$$\begin{array}{c} CO_2H \\ | \\ H-C-OH \\ | \\ H-C-OH \\ | \\ CO_2H \end{array}$$

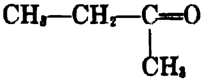
Meso-tartaric acid



$$\begin{array}{c} CO_2H \\ | \\ H-C-OH \\ | \\ HO-C-H \\ | \\ CO_2H \end{array}$$

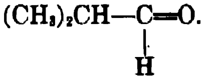
d- or *l*-Tartaric acid

6. An alkene A was prepared by the dehalogenation of an alkyl dihalide with zinc dust. The alkene was then treated with ozone to produce



$$CH_3-CH_2-\underset{\displaystyle CH_3}{\underset{|}{C}}=O$$

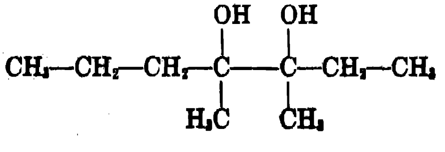
and



$$(CH_3)_2CH-\underset{\displaystyle H}{\underset{|}{C}}=O.$$

What would be the structure of the glycol obtained if the alkene A is oxidized with hydrogen peroxide in glacial acetic acid?

7. An alkene W was oxidized with $KMnO_4$ in aqueous Na_2CO_3 to yield



$$CH_3-CH_2-CH_2-\underset{\displaystyle H_3C}{\underset{|}{\overset{\displaystyle OH}{\overset{|}{C}}}}-\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle OH}{\overset{|}{C}}}}-CH_2-CH_3$$

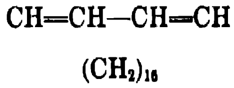
If the alkene W is treated with ozone and the resulting ozonide is hydrolyzed to yield two carbonyl compounds, what would be the structures of the two carbonyl compounds?

8. Given three unlabeled bottles A, B, and C, each containing a colorless liquid. The liquid in A is inert to aqueous $KMnO_4$, and it is identical to the compound produced by the reduction of isopentyl bromide with HI + phosphorus. The liquid in B is found to have a molecular formula of C_6H_{10}, adds *one* mole of Br_2 per mole of C_6H_{10}, and upon treatment of B with ozone and hydrolysis of the ozonide, one gets $O{=}CH{-}(CH_2)_4{-}CHO$. Compound C, also with molecular formula C_6H_{10}, adds *two* moles of Br_2 and gives a precipitate with ammoniacal silver nitrate. Deduce the structures of A, B, and C from these data.

9. Starting with 1,6-dibromo-5-methyl-3-hexene, what series of laboratory reactions would you use to prepare 1-methyl-1,3-cyclohexadiene?

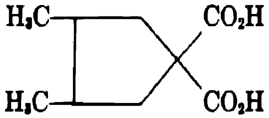
10. When a 1.65-g sample of a mixture of cyclohexane, cyclohexene, and 1-hexyne was reacted with excess bromine in the dark, it consumed 4 g of bromine. When an 0.825-g sample of the mixture of hydrocarbons was reacted with excess ammoniacal cuprous sulfate, 0.725 g of the cuprous hexynide (mol. wt. 145) was precipitated. What is the percentage by weight of the three hydrocarbons in the original mixture?

11. Starting with any desired aliphatic compound, indicate the series of laboratory reactions you would use to prepare



$$\begin{array}{c} CH{=}CH{-}CH{=}CH \\ (CH_2)_{16} \end{array}$$

12. Two geometric isomers (A and B) of 3,4-dimethyl-1,1-cyclopentanedicarboxylic acid (I) are possible. Draw their structures. Upon decarboxylation, isomer A yields two isomeric acids of 3,4-dimethylcyclopentanecarboxylic acid and B yields only one isomer. Assign structures to A and B.



I

6

Structure Determination by Physical Methods

We have seen so far that the alkenes, 1-alkynes, and saturated hydrocarbons can be separated or distinguished by chemical means on the basis of certain *differences* in their chemical properties. These chemical properties are associated with the types of functional groups present in their molecular structures. Indeed, one of the important steps involved in the identification, distinction, or structure determination of a given compound is to make an analysis for the types of functional groups present. This can also be done on the basis of certain physical properties. An empirical approach is generally used here. Organic chemists study in detail various properties of compounds whose structures are known, and they draw certain relationships between physical property and structure. These empirically developed generalizations are then used to deduce structures of new compounds or to add supporting evidence for previously proposed structures.

There are two advantages in the use of physical methods of analysis compared with chemical methods: (1) smaller-size samples are required for the physical methods, and (2) equilibrium mixtures may be studied without altering the equilibria. Nevertheless, a practicing chemist uses both methods in structure determination or functional group analysis, and after this chapter we shall use both techniques to complement each other as we study additional classes of compounds. It is too early to discuss some of the spectra-structure relationships; consequently, such a treatment is postponed until Chapter 21.

6.1 DIFFRACTION TECHNIQUES AND BOND DISTANCES

The most direct of the physical methods for structure determination when the experimental results can be interpreted is by diffraction. When a beam of X-rays (or electrons or neutrons) of a certain wavelength is allowed to impinge upon a sample, the beam is diffracted (scattered) by the atoms in the molecules much like dust particles reflect a beam of sunlight shining through the window. The reflected beam of X-rays produces a pattern on a photographic plate or other detector plate which must be interpreted in terms of the atomic arrangement within the sample. A complex equation has been developed which relates the intensity I of the scattered beam to the intensity I_0 of the initial beam. I is a function of all interatomic distances, nonbonded as well as bonded, and of the scattering angle ϕ.

Computations and approximation techniques are very arduous and require special training. Nevertheless, highly accurate results are obtainable, and bond distances and angles have been measured in thousands of molecules to an accuracy of ± 0.02 Å. Some common bond distances are given in Table 6.1. It must be emphasized that these values are those found in simple molecules.

TABLE 6.1. SOME COVALENT BOND LENGTHS

Bond-Type	*Length* (Å)	*Bond-Type*	*Length* (A)
C—C	1.53	C—O	1.43
C═C	1.335	C═O	1.20
C≡C	1.206	C—N	1.47
C—H	1.12	N—H	1.03
Arom. C—C	1.39	O—H	0.97

It has been found that four factors have marked effects on the length of a given bond-type, i.e., C—C, C—Cl, C═O, etc., in different molecules. Thus, resonance, hybridization, electronegativity, and steric requirements greatly influence bond distances in molecules. We will have an opportunity to observe the effects of some of these factors throughout the book.

The value and importance of diffraction measurements are shown by the fact that two Nobel Awards in chemistry were granted in recent years primarily for structure analysis of tremendously complex substances by diffraction techniques. Linus Pauling received the award in 1954, J. C. Kendrew and M. F. Perutz in 1962, and Dorothy C. Hodgkin in 1963.

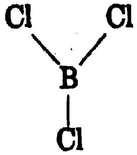
6.2 DIPOLE MOMENTS AND BOND DIPOLES

A body with negatively and positively charged ends is regarded as a dipole, even though it may not have a net positive or negative charge. A dipole arises, then, not from a net charge but from a *separation* of charge. The product of the magnitude of one of the poles (the center of positive or negative charge) times the distance between poles gives the dipole moment expressed in debye units. Thus, polar molecules are those which have a significant dipole moment.

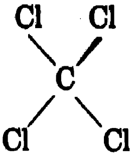
It is easy to understand that a difference in electronegativity of atoms A and B in the bond A—B would cause the electron cloud of the bond to be distorted with a larger electron density near the more electronegative atom. Hence, the bond becomes a dipole. Symmetrical molecules such as Cl_2, BCl_3, CCl_4, CH_4 and CO_2 do not have dipole moments:

$Cl—Cl$

Linear



Planar

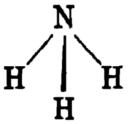


Tetrahedral

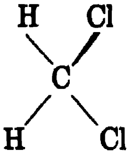
$O=C=O$

Linear

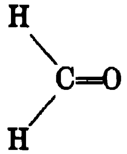
whereas unsymmetrical molecules such as NH_3, CH_2Cl_2 and H_2CO do have dipole moments:



Pyramidal

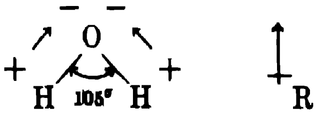


Tetrahedral



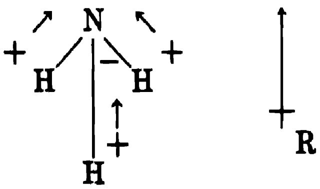
Planar

This led chemists to believe that bond dipoles are largely responsible for the dipole moments of polar molecules. Although bond dipoles are not the only sources contributing to dipole moments, empirical methods have been developed for assigning moments to various bond-types such that approximate moments can be computed for many molecules. For instance, the O—H bond moment is calculated from the observed dipole moment of HOH and the measured —O— bond angle:

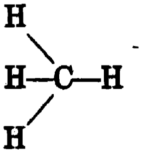


Resultant observed dipole moment = 1.84D

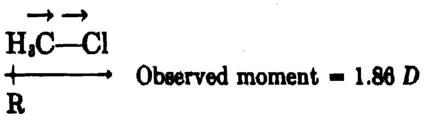
The arrows point from the positive to the negative poles. Similarly, the N—H bond moment may be calculated from the geometry and observed



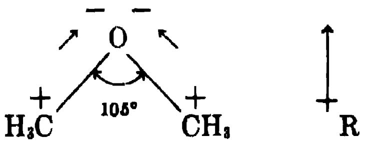
moment of NH_3, and the moments of the H—X bonds are taken as the moments of the respective hydrogen halides. Since methane has no moment, the H_3C group moment must have a magnitude equal to that of the C—H bond:



Then, the moment of the C—Cl bond can be computed from the measured dipole moment of CH_3Cl and an assigned C—H bond moment:



The C—O bond moment, for instance, may be computed from the moment observed for methyl ether and the C—H (equals the CH_3 group moment)



bond moment. In this fashion, bond moments have been worked out for various bond-types. Some values are given in Table 6.2.

TABLE 6.2. SOME BOND DIPOLE MOMENTS

Bond-Type (+ −)	*Bond Moment* (debyes)	*Bond-Type* (+ −)	*Bond Moment* (debyes)
H—C_{sp^3}	0.30	C—F	1.51
H—N	1.31	C—Cl	1.56
H—O	1.53	C—Br	1.48
H—F	1.98	C—N	0.40
H—Cl	1.03	C=N	0.90
H—Br	0.78	C—O	0.86
H—S	0.68	C=O	2.40
		N—O	0.30

The dipole moment of a molecule can give several types of information about its structure. For example, if a molecule has no dipole moment, it probably has a symmetrical structure. Or, if one can compute a dipole moment for a compound from the table of bond moments in agreement with the measured dipole moment, then one has increased confidence in the assigned structural formula. We shall see later that dipole moment data are used in support of resonance structures proposed for various molecules.

6.3 MOLECULAR ABSORPTION OF ENERGY

Light may be regarded as electric charges moving through space in a wave-like motion. As such, two ways of describing it are to give its wavelength and its frequency of vibration. The wavelength is the distance between two corresponding points on the path, and the frequency is the number of times that one wavelength is traversed per second. Obviously, the longer the wavelength, the lower is the frequency. The frequency of light determines its energy, and light of high frequency within the range called the *ultraviolet* is very powerful. It is capable of causing detrimental reactions within the human body, and since ultraviolet light is a component of sunlight, long exposures to sunlight are harmful to the skin. Sunburn, for example, is caused by the ultraviolet portion of sunlight, and from experience we know it can be very painful if too intensive. Light of low energy in the range called the *infrared* has a low frequency and long wavelength. That at the farthest end of this range is nothing more than heat energy. It has beneficial effects toward certain body ailments and is used extensively in physical therapy.

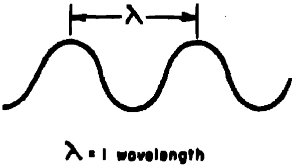


Fig. 6.1.

TABLE 6.3. WAVELENGTHS OF VARIOUS REGIONS OF THE ELECTROMAGNETIC SPECTRUM

Region:	Cosmic Rays	γ-ray	X-ray	Ultra-violet	Visible Light	Infrared (Heat)	Micro-wave	Radar	Radio
Wavelength: (A°)			1		4000 8000	10^6	10^8	10^9	10^{14}

1 Å = 10^{-8} cm

The portion of the spectrum of greatest use to chemists extends from the ultraviolet to the microwave region. When a molecule is exposed to a light source, it may absorb some of the light energy and certain changes will occur within the molecule. Absorption of energy from the far infrared or microwave regions will produce certain types of atom or group rotations within the molecule. Absorption of energy from the lower end of the infrared region can produce various modes of atom or group vibrations plus the rotations mentioned above. Absorption of light energy from the ultraviolet or visible regions of the spectrum produces changes in the electronic energy of the molecule in addition to vibrational and rotational changes. Changes in electronic energy correspond to alterations in electron configurations.

A chemist studies these changes in internal energy through spectroscopy. A sample is placed between the source of radiation and a recorder. A prism, grating, or other device is used to resolve the light source into its component wavelengths. A photographic plate or photoelectric cell serves as a recorder for the ultraviolet and visible regions, and thermopiles or bolometers are used for the infrared region. A spectrum of the compound is obtained by hand-plotting or automatically recording the relative amounts of absorption of energy at the various wavelengths against the values of the wavelengths themselves. The units of wavelength are commonly replaced by their reciprocals, *wave numbers*, for the infrared region. Spectra are designated ultraviolet, visible, infrared, microwave, etc., depending upon the region in which they are measured. No one form of spectroscopy is universally best; each is used to complement the others.

Spectroscopy has become the most widely used tool in chemistry today. It provides quick, highly accurate analyses for guidance in research and industry, it has contributed to the fundamental knowledge about chemical bonding in molecules, and it has led to the elucidation of the structures of complex organic and inorganic substances. It is standard procedure now to give certain spectral characteristics of newly isolated or synthesized compounds as a means of their future identification. Consequently, mention will be made throughout the text of the application of spectroscopy to a particular problem.

6.4 INFRARED SPECTROSCOPY AND FORCE CONSTANTS

A good analogy of a covalent bond is to regard it as a metal spring holding together two charged balls. Each type of springlike bond has its own unique elasticity or natural-vibrational frequency. When a ray of light of this same frequency passes the molecule, the molecule absorbs some of the incident energy which can be recorded by a spectrophotometer. By studying a large number of compounds, chemists observed that certain frequency ranges can be associated with certain bond-types. Some of these values are listed in Table 6.4.

TABLE 6.4. INFRARED ABSORPTION FREQUENCY RANGES FOR SOME BOND-TYPES

Bond-Type	*Frequency Range*	*Bond-Type*	*Frequency Range*
$H—C_{sp^3}$	2850–2960 cm^{-1}	C—O	1060–1270 cm^{-1}
$H—C_{sp^2}$	3010–3040	C—F	1000–1400
$H—C_{sp}$	3250–3300	C—Cl	600– 800
C═C	1620–1680	C—Br	500– 600
C═O	1650–1825	O—H	3590–3650
C≡C	2100–2260	N—H	3300–3500
C≡N	2215–2260	S—H	2500–2600

Following the analogy given above, a molecule can be pictured as a mechanical system of balls all interconnected by springs of different tensile strengths. When one bond is set into vibration, the entire system is affected, and the specific resonant frequency for a given bond will depend upon the entire molecule. Thus, the C—H— does not exhibit precisely the same absorption frequency in all molecules. Fortunately, the range of frequencies for each bond-type is sufficiently narrow so that an observed band can usually be assigned to a certain bond-type. Also, a given bond may undergo several types of vibrations, i.e., it may stretch, bend, or do this in phase or out of phase with other atom vibrations. Each different mode of vibration requires a different quantity of energy to produce a unique absorption peak. Accordingly, an infrared absorption spectrum may be quite complex. See Figures 3.3 and 21.1.

The resistance to stretching or bending of a bond is noted not only by the quantity of energy required to do so but also by the force required. It is well known that when a metal spring is stretched, the more it is stretched the harder it is to stretch it further. That is, the force to stretch it is proportional to the distance stretched. This is expressed mathematically as

$$F \propto x \quad \text{or, better,} \quad F = -kx$$

where F is the force needed to stretch the bond a distance x, and k is a constant relating the two variables, called the *force constant.* Force constants are determined experimentally from Raman spectra.

When a beam of light passes through a transparent medium and the reflected light is viewed at right angles to the incident beam, some of the original light rays will be found to have shifted wavelengths. Sir Raman, an Indian physicist, was able to show that the spectra of the scattered light, called Raman spectra, can be attributed to atomic oscillations in the molecules and that bond force constants could be computed from the frequency shifts.

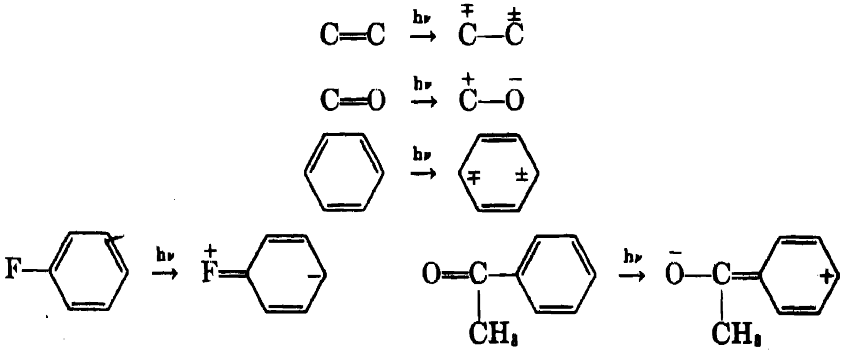
Force constants are in different ranges for single, double, and triple bonds:

Single bonds	$<7 \times 10^5$	dynes/cm
Double bonds	$7\text{–}15 \times 10^5$	dynes/cm
Triple bonds	$>15 \times 10^5$	dynes/cm

This generalization can be used to provide supporting evidence for the bond character of a given bond in a molecule. For example, the bond force constants of the carbon-carbon bonds in benzene are all identical, 7.6×10^5 dynes/cm, which is between the values for the ethane C—C bond, 4.5×10^5, and the ethylene C=C bond, 9.8×10^5 dynes/cm. This is in agreement with the resonance structure and the molecular orbital structure of benzene discussed in the next chapter.

6.5 ULTRAVIOLET SPECTRA AND CHROMOPHORES

The absorption of light from the ultraviolet-visible range of the spectrum excites valence electrons. These excitations or electronic transitions are described in terms of structural formulas as follows, where hν represents the absorption of light:



$$\mathrm{C{=}C} \xrightarrow{h\nu} \overset{\mp}{\mathrm{C}}\text{—}\overset{\pm}{\mathrm{C}}$$

$$\mathrm{C{=}O} \xrightarrow{h\nu} \overset{+}{\mathrm{C}}\text{—}\overset{-}{\mathrm{O}}$$

The excited states are thought to resemble the polar structures. The less energy required for these transitions, the longer is the wavelength at which light absorption occurs. This will depend upon the polarizability of the electrons involved, which normally decreases in this order: nonbonding, pi, and sigma electrons.

Each bond-type has a characteristic excitation energy and exhibits absorption bands at certain wavelengths, designated λ_m. Since all colored compounds contain one or more unsaturated groups, these linkages are called *chromophores* (Gr. *chrome*, color, plus *phoros*, bearer). As the chromophores absorb light of longer and longer wavelength (smaller and smaller energy) the color-producing power of the chromophores increases (Table 6.5).

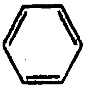
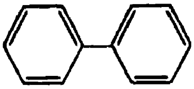
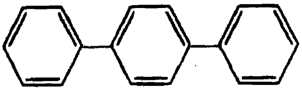
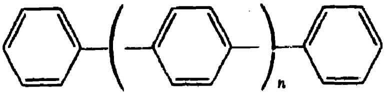
TABLE 6.5. ABSORPTION WAVELENGTHS OF SOME CHROMOPHORES

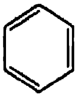
Group	Example Compound	Wavelength (Å)	Visible Color
C=C	$H_2C{=}CH_2$	1800	Colorless
C=N	$(CH_3)_3C{-}CH{=}N{-}C(CH_3)_3$	2500	Colorless
C=O	$(CH_3)_2C{=}O$	2800	Colorless
N=N	$CH_3{-}N{=}N{-}CH_3$	3470	Pale yellow
C=S	$(CH_3)_2C{=}S$	4000	Light yellow
N=O	$CH_3CH_2CH_2CH_2{-}N{=}O$	6650	Blue-green

Conjugation of chromophores increases the polarizability of the valence electrons, and leads to absorption at longer wavelengths. For illustration, the color of the diphenylpolyenes, $\phi{-}(CH{=}CH)_n{-}\phi$, deepens as n increases (cf. Figure 2.6 and Table 6.6). Similarly, the color of polynuclear compounds increases as the extension of the conjugated system increases. Two illustrations are given on the next page.

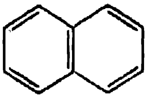
TABLE 6.6. COLOR AND LIGHT ABSORPTION OF DIPHENYLPOLYENES, $\phi{-}(CH{=}CH)_n{-}\phi$

Value of n	Color of Compound	Wavelength of Principal Absorption in Benzene (Å)
1	Colorless	3190 and 3060
2	Colorless	3520 and 3340
3	Pale yellow	3770 and 3580
4	Green-yellow	4040 and 3840
5	Orange	4240 and 4030
6	Brown-orange	4450 and 4200
7	Red-orange	4650 and 4350
11	Violet-black	5300 and 4930
15	Green-black	5700 and 5320

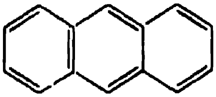
		λ_m(Å)
	Benzene	2030
	Biphenyl	2515
	Terphenyl	2800
	*para*-Polyphenyls	
	$n = 2$	3000
	$n = 3$	3100
	$n = 4$	3175



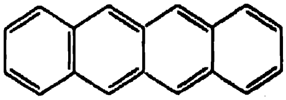
Benzene
colorless
$\lambda_m = 2030$ Å



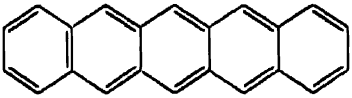
Naphthalene
colorless
$\lambda_m = 3140$ Å



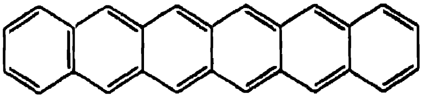
Anthracene
buff color
$\lambda_m = 3800$ Å



Naphthacene
yellow
$\lambda_m = 4800$ Å



Pentacene
blue
$\lambda_m = 5800$ Å



Hexacene
green
$\lambda_m = 6000$ Å

Some groups do not make molecules colored, but increase the coloring power of chromophores. These groups are called *auxochromes* (Gr. *auxo*, increase). The most common auxochromes, listed in decreasing effectiveness, are $—NR_2$, $—NH_2$, —OH, $—OCH_3$, —X, —R, where X is a halogen and R is a saturated alkyl group. For illustration, polyaminobenzenes are colorless because the NH_2 group does not impart color, and nitrobenzene is colorless because the color-producing power of one NO_2 group is too weak to impart color. However, nitroanilines ($O_2N—C_6H_4—NH_2$) are yellow because the NH_2 group increases the color-producing effect of the NO_2 group.

There may be more than one absorption band in the UV spectrum of a molecule because several types of electronic transitions may occur. Thus, absorption bands can be observed for excitation of pi or lone-pair electrons to antibonding orbitals, called $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions, respectively, or for excitation of the electrons in different chromophoric systems in a molecule, or even for transitions to higher excited states. For example, 2-methoxy-5-nitroaniline has four absorption bands in neutral or basic solutions (Figure 6.2). Two of these bands, λ_m and λ''_m, must involve the lone-pair

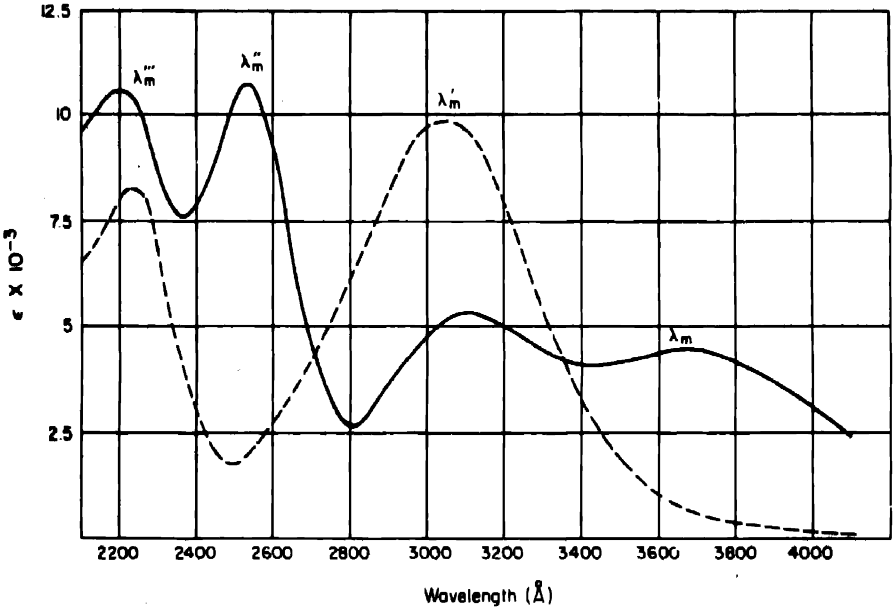
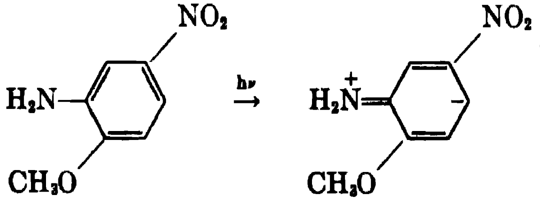
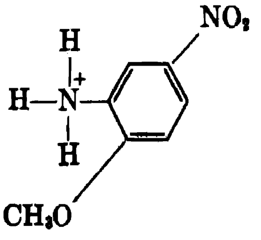


Fig. 6.2. Ultraviolet spectrum of 2-methyl-5-nitroaniline in 0.1N NaOH (——) and in 0.1N H_2SO_4 (- - -).

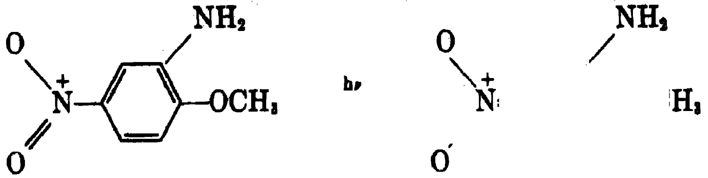
electrons of the amino group because these two bands disappear when the compound is placed in acid solution wherein the former lone-pair electrons are no longer available for easy excitation.





No lone-pair electrons on NH_3

Band λ'_m is associated with the excitation



and λ'''_m is believed to be associated with an excitation of just the benzene ring electrons.

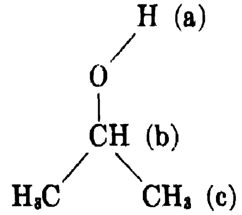
It is noteworthy that the physical properties discussed earlier provide information about fundamental characteristics of a covalent bond, such as the energy, length, force constant, dipole moment, and infrared absorption frequency of a bond. These properties are all directly or indirectly related to one another, and often one is derived from the others. Ultraviolet spectra, on the other hand, do not provide information about individual bonds; rather, they are characteristic of the systems of multiple bonds over which the electronic system is excited. Because of the geometric requirements of multiple bonds, the spectra reflect the extent of conjugation of multiple bonds, intramolecular spatial crowding of groups (steric hindrance), hydrogen bonding, and other structural features to be taken up later.

6.6 NUCLEAR MAGNETIC RESONANCE SPECTRA

Nuclear magnetic resonance spectroscopy, n.m.r., is one of the newer methods used by organic chemists and has become one of the most powerful and versatile tools available. Atomic nuclei spin and precess in a magnetic field like rotating tops in the gravitational field, and certain atoms have residual magnetic moments. When one of these magnetic nuclei is placed in a magnetic field, it can assume relative orientations with respect to the field which differ in energy. If an alternating magnetic field is superimposed upon the stationary field, there will be an absorption of energy by the nucleus when the frequency (energy) of the alternating field matches the excitational energy between the lower and higher energy states (orientations) of the nucleus. For protons in a field of 14,092 gauss, for example, this "resonance" frequency is 60 Mc (megacycles). Now, since electrons revolve around nuclei, the rotating charges produce miniature magnetic fields which oppose the external magnetic field and therefore partially reduce the external field strength on the nucleus, i.e., they partially *shield* the nucleus from the full force of the external field. This shielding effect is related to the degree to which the electrons stay close to the nucleus, i.e., increases with the *s* character of *s-p* hybrid bonds and with the electronegativity of the atom. This magnetic effect is only exhibited by certain types of atoms, P^{31}, F^{19}, Cl^{35}, C^{13} (but not C^{12}), and H^1. In practice, the n.m.r. spectrum for a given-type atom, i.e., H^1, F^{19}, etc., is measured for a given compound, and the position of absorption is compared with that of a reference compound. The difference in the positions of the peaks is called the *chemical shift*, δ

$$\delta = \frac{H_R - H_S}{H_R} \text{ p.p.m.}$$

where H_R and H_S are the field strengths required for absorption by a given type atom in the reference compound and the same type atom in the sample. Since the electronegativity of a specific atom is influenced by the type and position of neighboring atoms, the chemical shifts of chemically nonequivalent atoms will differ. That is, *n*-propane has two sets of equivalent protons, those on the C_1 and C_3 atoms are all equivalent, and the two on the C_2 atom are equivalent. Isopropyl alcohol has three types of protons, the hydroxyl protons (a), the proton on the middle carbon atom (b), and one of the methyl protons (c). Each type exhibits a different chemical shift, and the relative intensities of the absorption peaks are in the ratio a:b:c = 1:1:6.



Furthermore, these magnetic nuclei become "coupled" to neighboring nuclei via bonding electrons to produce "splitting" of the principal resonance peaks. As a first approximation, there will be $n + 1$ "teeth" in a proton absorption band, where n is the number of protons attached to atoms in α positions. For illustration, for the three types of protons in CH_3CH_2OH, the band for the CH_3 protons has three peaks from coupling with the two CH_2 protons, the band for the CH_2 protons has four peaks from coupling with the three CH_3 protons, each of the four peaks has two teeth from coupling with the OH proton, and finally, the OH proton band has three peaks from coupling with the two CH_2 protons. The magnitude of the splitting, called the coupling constant J (spread of the teeth), depends upon the number, types, and orientations of chemical bonds separating the coupled nuclei. Consequently, n.m.r. spectra are examined for chemical shifts and the heights and splitting of peaks. These characteristics are then interpreted in terms of molecular structure. An n.m.r. spectrum is illustrated in Figure 6.3.

6.7 MASS SPECTROSCOPY

Mass spectroscopy is one of the most recently discovered physical techniques used by organic chemists for structure analysis.

A sample is vaporized in a mass spectrometer and bombarded with an electron

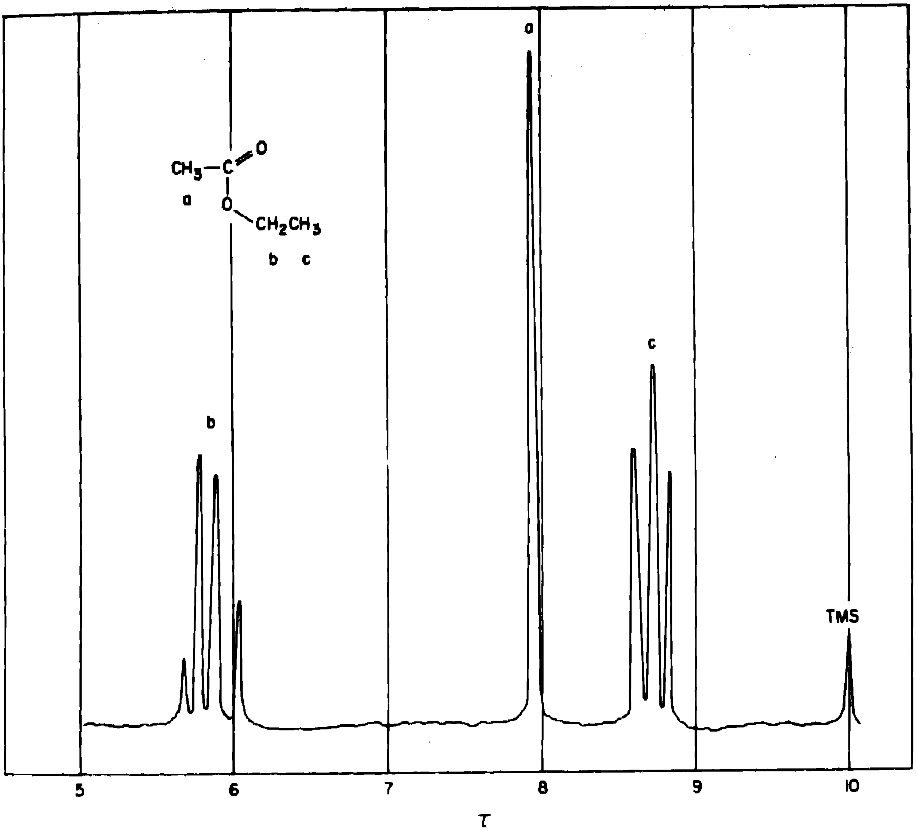
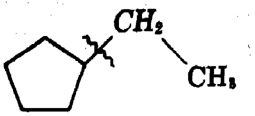


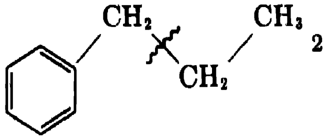
Fig. 6.3. N.m.r. spectrum of ethyl acetate at 60 Mc. TMS = tetramethylsilane internal standard.

beam. This not only ionizes the molecules but breaks them up into ionized fragments. The positive ions are passed into a magnetic field and follow a circular path whose radius depends upon the ratio of their mass to charge (m/e) for each particle. Thus, for a given charge, they are separated on the basis of mass. A single electron removed from the initial molecule produces the *parent ion*, and this species gives a highly accurate value of the molecular weight of the sample. This ion is also usually present in the largest amount. The spectrum, then, consists of the m/e values for the various fragments plotted against their relative abundances. The largest peak is called the *base* peak and is assigned a value of 100, and the other peaks are reported as percentages of the base peak. A mass spectrum is often presented as a two-column table; one column gives the m/e values for the principal peaks in the spectrum and the other column gives the "per cent of base peak."

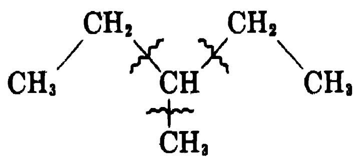
A mass spectrum provides not only the molecular weight of a sample but also the molecular weight of its principal degradation fragments. Again, by observing the manner in which known structures tend to break up, several empirical rules have been developed regarding the fragmentation of molecules. For example, some simple rules are the following:



1. **Saturated rings tend to lose side chains at the *alpha* carbon atom.**



2. **In an alkylbenzene, cleavage is most probable at the bond *beta* to the aromatic ring.**



3. **Cleavage is favored at branched carbon atoms.**

By identifying the fragments through their particle weights and by the use of these and other empirical rules, the structure of an unknown compound may be deduced or confirmed from its mass spectrum.

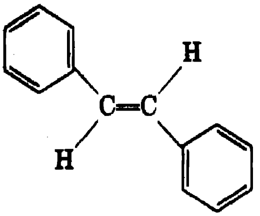
TEST QUESTIONS, Set 6

1. Carbon dioxide has no dipole moment but sulfur dioxide does. Propose structural formulas for these two compounds on this basis.

2. How do you account for the fact that CCl_4 and CH_4 have no dipole moments but CH_3Cl does?

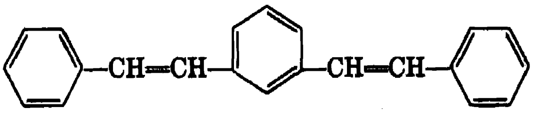
3. If CH_3Cl were planar, would it have a dipole moment?

4. How do you account for λ_m (the wavelength at maximum intensity of an absorption band) of compound I being about the same as that of compound II? Would you predict a similar λ_m for compound III?



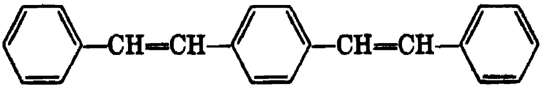
I

$\lambda_m = 295\ m\mu$



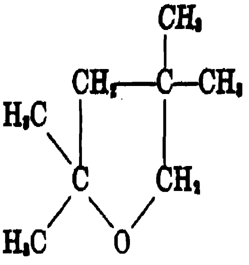
II

$\lambda_m = 298\ m\mu$



III

5. How many groups of nonequivalent protons are there in compound IV, and what is the ratio of the number of protons in each group? Should the peaks be singlets or multiplets?



IV

6. The compound C_6H_5—CH(CH_3)—O—CH(CH_3)—C_6H_5 has three n.m.r. proton peaks at 2.82 τ, 5.56 τ, and 8.57 τ. Assign these peaks to the protons in the compound and predict the multiplicity of each peak.

7. Like ethyl acetate (Figure 6.3), methyl propionate has a singlet, triplet, and a quartet in its n.m.r. spectrum. How could the two isomeric compounds be distinguished by their n.m.r. spectra?

7

Benzene and Aromatic Character

Benzene is generally regarded as the parent of aromatic carbocyclics and is produced in the largest amount. At one time, coal was the major source of aromatic chemicals; but in the past 20 years, petroleum has become the principal source of several commercially important aromatic hydrocarbons. Since one-third of all organic chemicals are derived from coal, a brief discussion on coal is appropriate.

7.1 PYROLYSIS OF COAL

As a result of slow decomposition beginning some 300 million years ago, and under the effects of moisture, high temperature and pressure, and little air, buried plants were changed into various carbonaceous residues. These have been in the form of gases (natural gas), liquids (petroleum), and solids (coal, shale rock, tar sands, etc.). The solids are of varying carbon content.

	Per Cent Carbon
Peat	11
Lignite (brown coal)	35
Bituminous (soft coal)	65
Anthracite (hard coal)	85
Diamond	100

Bituminous coal is the most abundant. Coal deposits are unevenly distributed in the earth's crust. Most major deposits seem to be in the temperate zones. Asia has about a third, and North and South America more than half of the world's coal reserves. England has turned to digging for coal beneath her surrounding seas just as the United States is drilling oil wells beneath her coastal areas. It appears that coal is derived from land plants, and petroleum from marine organisms. The carbon skeletons form unsaturated rings in coal and mostly open saturated chains in petroleum.

For a number of years, coal was converted to coke by being heated in big ovens in the absence of air (pyrolysis). The coke was used in the metallurgical industries as a source of heat and for the reduction of ores. A little less than a century ago, chemists learned that valuable dyes, medicinals, explosives, and many other chemicals could be obtained from the liquefiable distillate in the coking process. In 1907, Dr. Heinrich Koppers developed the first apparatus and method in this country for the economical recovery of chemicals produced from coal in the coking process, and what had been a by-product grew into a treasure storehouse for the chemical industry. Some of the initial products of the coal-tar industry are summarized in Table 7.1.

TABLE 7.1. PRODUCTS FROM THE PYROLYSIS OF ONE TON OF COAL

COAL
- → 20 lb. ammonium sulfate
- → 11,000 cu. ft. illuminating gas (52% H_2, 32% CH_4, 7% CO)
- → 3 gal. light oil 65% benzene
  - 15% toluene
  - xylenes, thiophene, etc.
- → 8 gal. coal tar: fractionated to yield
  - Middle oil (naphthalene
    - phenol
    - pyridine)
  - Heavy oil (cresol, etc.)
  - Anthracene oil (anthracene, creosotes)
  - Pitch (the residue; used for roofing and paving roads)
- → 1500 lb. coke

The process consists in heating coal near 1000° in the absence of air. The volatile substances are passed through a condenser into a sulfuric acid "scrubbing solution." This dissolves out the ammonia and hydrogen sulfide, while the illuminating gas, also called *coke-oven gas*, passes on. The organics form separate layers—one which floats on the sulfuric acid, called *light oil*, and a second, black, foul-smelling liquid which settles to the bottom, called *coal tar*.

Twenty pounds of ammonium sulfate from one ton of coal may seem like a small amount, but when one realizes that over 100 million tons of coal are coked a year, it is seen that more than a million pounds of ammonium sulfate are obtained annually from this source. Illuminating gas is now used largely as a source of heat. The organics obtained from coal tar will be referred to as the respective classes are taken up.

7.2 STRUCTURE OF BENZENE

Benzene was discovered by Faraday in 1825 from condensates in pipes used for conducting coke-oven gas. Its formula was determined by Mitscherlich in 1834, and he named it *benzin*. Liebig preferred to call it *benzol*, and his greater influence is evident since the German name is still benzol. To avoid confusion with alcohols, the *-ol* ending was changed to *-ene* by the British, so that benzene is its name in English. Later, in 1845, Hofmann obtained benzene from coal tar.

The degree of unsaturation of hydrocarbons is indicated by the C/H ratio. We have for the alkanes C_nH_{2n+2}; for the alkenes C_nH_{2n}; and for the alkynes C_nH_{2n-2}. Hence, the formula of benzene, C_6H_6, which fits the formula C_nH_{2n-6}, suggests a high degree of unsaturation comparable to that of acetylene (C_2H_2). However, when the properties of benzene are compared to those of typical unsaturated aliphatics or alicyclics, it is seen that benzene is very unusual. Such a comparison is made in Table 7.2.

TABLE 7.2. COMPARISON OF PROPERTIES OF ALKENES AND BENZENE

Alkenes	*Benzene*
1. Oxidized rapidly by cold permanganate or concentrated nitric acid.	1. Stable to permanganate or concentrated nitric acid at moderate temperatures.
2. Add halogens and H_2SO_4 at 0°.	2. Unreactive to halogens and H_2SO_4 at 0°.
3. Easily polymerized	3. Does not polymerize.
4. Undergo *addition* reactions.	4. Undergoes *substitution* reactions.

The reactions of benzene are typically those of aromatic compounds, provided substituents themselves do not undergo the olefinic reactions. Thus, compounds whose formulas reveal unsaturation, but which do not exhibit the typical unsaturation properties of alkenes, are said to have *aromatic character*. The greater the difference in properties from those of alkenes, the greater is the aromatic character of a compound. Note that aromatic character has no reference to the fragrance of a substance.

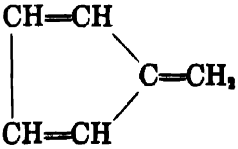
One of the most perplexing problems facing chemists has been the structure of the nucleus of benzene. Several structures may be worked out for C_6H_6, such as:

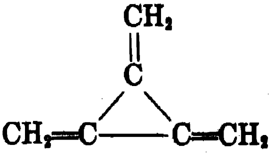
$CH_2{=}CH{-}C{\equiv}C{-}CH{=}CH_2$

$CH_3{-}C{\equiv}C{-}C{\equiv}C{-}CH_3$

$CH_3{-}C{\equiv}C{-}CH_2{-}C{\equiv}C{-}H$

$HC{\equiv}C{-}CH_2{-}CH_2{-}C{\equiv}CH$



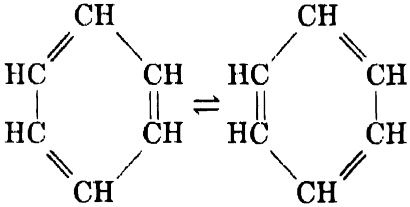


However, there is no reason why any of these should not be easily oxidized by permanganate or why they should not exhibit any of the olefin properties. In Section 1.4 it was pointed out that, in 1858, Kekulé introduced the notion of the quadrivalence of carbon and that single and multiple bonds between carbon atoms may occur in order to maintain this quadrivalence. In 1865 Kekulé proposed a cyclic structure for benzene, one of the most important contributions ever made to organic chemistry. Although his idea is not accepted completely today, it started chemists of his day thinking along entirely new lines which led to a rapid development of organic chemistry.

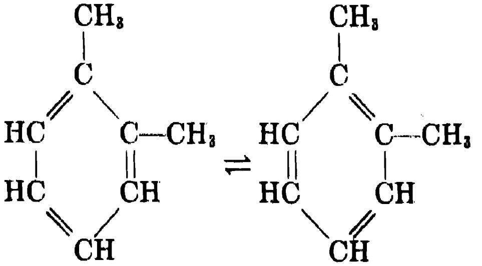
Friedrich August Kekulé (1829–1896), one of the most important figures in the history of organic chemistry, was a pupil of Liebig (1803–1873). Kekulé was a great teacher and attracted many students, among whom were Van't Hoff (1852–1911), first Nobel Prize winner in chemistry; Emil Fischer (1852–1919), second Nobel Prize winner in chemistry; von Baeyer (1835–1917), fifth Nobel Prize winner in chemistry; and Victor Meyer (1848–1897), a leading organic chemist of the nineteenth century. Kekulé's part in the training of such illustrious chemists alone is noteworthy.

Kekulé's proposal for a dynamic structure of benzene was seeded by a dream. He had been working on his textbook when he turned his chair to the fireplace for a moment's rest. He fell "half asleep," whereupon he visualized rows of atoms moving in twisting, snakelike motions. Suddenly, one of the snakes seized its own tail. Kekulé "awoke as by a flash of lightning" and spent the remainder of the night translating his dream into two interchanging hexagons of carbon and hydrogen atoms (see below).

Kekulé's structure (1866):



Kekulé proposed alternate single and double bonds around a six-membered ring and held the notion that the bonds flipped back and forth, giving rise at any instant to the presence of two types of molecules. These would be indistinguishable for benzene, but for a disubstituted benzene, such as *o*-xylene, $C_6H_4(CH_3)_2$, there should be two distinguishable isomers.

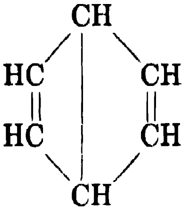


Kekulé's structure for *o*-xylene

One isomer has a single bond, and the other a double bond between methylated carbon atoms. However, not only was it hard for chemists to accept the idea of dynamic structures in contrast to static structures, but also no evidence for two different *o*-xylenes could be found. Consequently, Kekulé's structures were not completely accepted, and many others were proposed over the next fifty years. Some of these will be mentioned here.

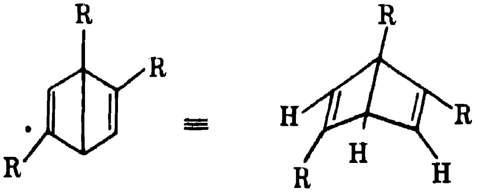
Benzene was known to give only one monosubstitution product; hence, its six hydrogen atoms must be equivalent. Therefore, most proposals were based on some sort of cyclic structure.

Dewar's structure (1867):



If benzene had this structure, the long bond and the double bonds should make it reactive like alkenes. Also, the bonding would not differ between adjacent and opposite carbon atoms of the ring; therefore, only two disubstitution isomers would be possible. Hence, Dewar's structure predicts properties contrary to fact.

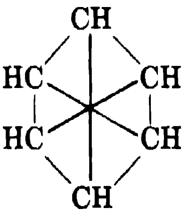
Recently a hydrocarbon with a Dewar-type structure was isolated.[1]



R = *t*-butyl

However, the isolated compound does not have a planar structure as observed for benzene and its derivatives and proposed by Dewar.

Claus' structure (1867):



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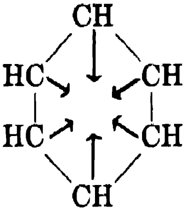
[1] E. E. Van Tamelen and S. P. Pappas, *J. Am. Chem. Soc.* **84**, 3789 (1962).

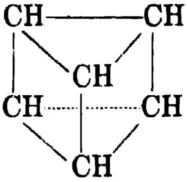
The objections to this structure are essentially the same as those against the Dewar structure.

Armstrong-Baeyer's centric structure (1867):



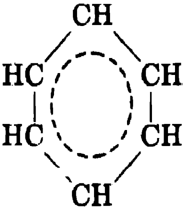
Each carbon has its fourth bond directed toward the center of the ring. The idea was that, having its fourth valence pointed inward, each carbon was chemically inert, thus accounting for the inertness of benzene. However, if this were the structure, the fourth valence of each carbon should be independent of the other five radial bonds, and benzene should react to form C_6H_6X products, where X is any group. Since benzene never forms such compounds, this structure was rejected.

Ladenburg's prism structure (1869):

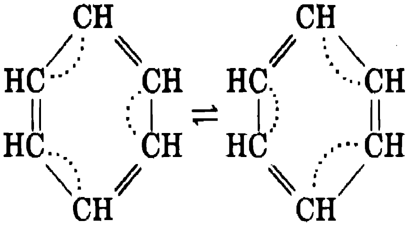


This structure was proposed to account for the inertness of benzene. However, with this structure, a trisubstituted benzene, $C_6H_3X_3$, would have no plane of symmetry, no matter which positions the groups held. The lack of a plane of symmetry would produce optical isomers, but trisubstituted benzenes are not optically active, provided the substituents themselves are not asymmetric. Hence, the Ladenburg structure was not acceptable.

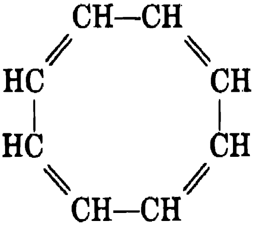
Thiele's structure (1899):



Thiele's theory of partial valences held that the residual valences of the C_2—C_3 bond of a conjugated system are tied up through mutual neutralization to diminish the reactivity of these two carbon atoms. This would occur, also, across the single bonds of the two Kekulé structures.

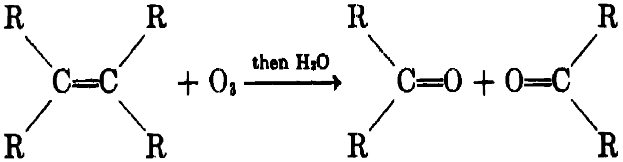


Thiele combined these two alternatives into his single structure given above. He thought that the closed conjugated system around the ring makes all of the carbons inert, giving the compound aromatic character. However, about a decade later, cyclooctatetraene was synthesized.

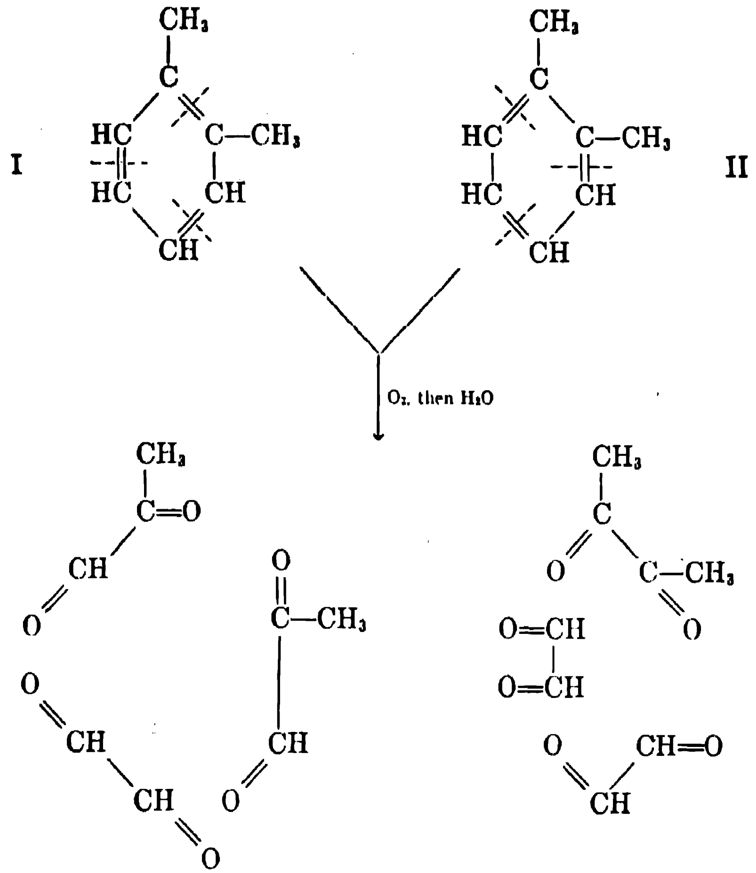


It, too, has a closed conjugated system around the ring; therefore, according to Thiele's idea, cyclooctatetraene should have aromatic character. To the contrary, it is a very reactive cycloolefin.

Not long after this, ozonolysis experiments with aromatic hydrocarbons provided strong evidence for Kekulé's structures. Recall that ozone reacts with olefinic bonds to cleave them and change the olefinic carbons to carbonyl groups.



If ozone were to react with *o*-xylene, for example, and if *o*-xylene had the Kekulé structures, the following products should be formed.



For each mole of *o*-xylene reacting, there would be the following *molar ratio* of products from structures I and II:

	$H-\underset{\substack{\Vert\\ O}}{C}-\underset{\substack{\Vert\\ O}}{C}-H$		$H-\underset{\substack{\Vert\\ O}}{C}-\underset{\substack{\Vert\\ O}}{C}-CH_3$		$H_3C-\underset{\substack{\Vert\\ O}}{C}-\underset{\substack{\Vert\\ O}}{C}-CH_3$
I	1		2		0
II	2		0		1
	—		—		—
Molar ratio:	3	:	2	:	1

Note that if only structure I were present, no $H_3C-CO-CO-CH_3$ would be produced, whereas if II were the only structure, no $H-CO-CO-CH_3$ would be produced. In order to get all three products, both structures I and II must be present. If I and II exist in equal amounts, the molar ratio of products should be 3:2:1. Within experimental error, this is exactly the ratio in which the products are obtained in the actual ozonolysis of *o*-xylene. Ozonolysis of other aromatic compounds gave similar results in support of Kekulé's structures.[2] This seemed to be convincing evidence for the Kekulé structure—one of the earliest structures proposed for the benzene nucleus.

In the 1920s, chemists began to study the physical properties of compounds to a greater extent. Among these were the absorption of light energy, heats of combustion, X-ray diffractions, and dipole moments. From heats of combustion, one may determine the chemical potential energy or chemical stability of compounds; i.e., the energy tied up in their chemical bonds. For illustration, chemists set the *natural* form of the elements as reference points. Thus, the heat liberated when a compound is formed from its elements is its *heat of formation*. The heats of formation of CO_2 and H_2O, then, are the heats liberated when these two compounds are formed from their elements. Now, when methane is burned, CO_2, H_2O, and heat are produced. Knowing the amount of chemical energy tied up in CO_2 and H_2O, one may calculate the chemical stability of methane from its heat of combustion. This is the chemical energy contained in four C—H bonds. One-fourth of this value is taken as the C—H bond energy. Similarly, the chemical stability of ethane may be computed from its heat of combustion. One subtracts six times the C—H bond energy from the potential energy of ethane to get the C—C bond energy. Similar treatments to $CH_2{=}CH_2$ and $HC{\equiv}CH$ will give the C═C and C≡C bond energies. This was done for many compounds, and a set of bond energies was established for most of the types of covalent bonds, C—O, C—N, C═O, etc. Some of the common values are given in Table 7.3. From this table, one may calculate the chemical stability of a covalent compound, which should not

TABLE 7.3. SOME COVALENT BOND ENERGIES

Bond	Bond Energy (kcal./mole)	Bond	Bond Energy (kcal./mole)
C—C	80	C═C	145
C—H	98.2	C═O	179
C—O	88	C═N	153
C—N	78	N═N	152
C—Cl	78	S═O	120
O—H	109.4	C≡C	198
N—H	92.2		

CHEMICAL STABILITIES* (kcal./mole)

O_2	146.2	$H_2O_{(liq.)}$	244.9
CO_2	410.7	N_2	278.2

* These values are adjusted so that use of bond energies from this table give reasonable results.

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[2] N. Campbell, *Ann. Reports Chem. Soc. London* **44**, 127 (1947).

be far from the experimental value if the calculation is based upon the correct structure. For illustration, from the measured heat of combustion of trimethylamine, 588 kcal/mole, and from the chemical stabilities of the other substances in the reaction,

$$2(CH_3)_3N + 10\tfrac{1}{2}O_2 \rightarrow 6CO_2 + 9H_2O + N_2 + 1176\text{ kcal}$$

one may compute the chemical stability of trimethylamine:

$$\Delta H = E_{\text{products}} - E_{\text{reactants}}$$

$$\Delta H = 6E_{CO_2} + 9E_{H_2O} + E_{N_2} - 2E_{(CH_3)_3N} - 10.5E_{O_2} = 1176\text{ kcal}$$

where E is the chemical stability of a given compound.

$$\begin{aligned}\therefore 2E_{(CH_3)_3N} &= 6E_{CO_2} + 9E_{H_2O} + E_{N_2} - 10.5E_{O_2} - 1176\\ &= 6(410.7) + 9(244.9) + 278.2 - 10.5(146.2) - 1176\\ &= 2236\\ E_{(CH_3)_3N} &= 1118\text{ kcal}\end{aligned}$$

The value from the bond energies in Table 7.3 is

$$9(C{-}H) + 3(C{-}N) = 9(98.2) + 3(78) = 883.8 + 234 = 1118\text{ kcal}$$

Such calculations for benzene derivatives, using Kekulé's structure of the nucleus, are always too low. For illustration, from the bond energies listed in Table 7.3, the calculated chemical potential energy for one of the Kekulé structures of benzene is:

$$\begin{aligned}\Delta H_{\text{calc.}} &= 6(C{-}H) + 3(C{-}C) + 3(C{=}C)\\ &= 6(98.2) + 3(80) + 3(145) = 1264\text{ kcal/mole}\end{aligned}$$

The experimental heat of combustion of benzene is 792 kcal, so that from the equation,

$$C_6H_6 + 7\tfrac{1}{2}O_2 \rightarrow 6CO_2 + 3H_2O + 792\text{ kcal}$$

the chemical potential energy of benzene is found to be as follows:

$$\begin{aligned}\Delta H &= 6E_{CO_2} + 3E_{H_2O} - E_{C_6H_6} - 7.5E_{O_2} = 792\\ E_{C_6H_6} &= 6E_{CO_2} + 3E_{H_2O} - 7.5E_{O_2} - 792\\ &= 6(410.7) + 3(244.9) - 7.5(146.2) - 792 = 1300\text{ kcal/mole}\end{aligned}$$

Thus, the measured chemical stability, 1300 kcal/mole, is greater than the calculated value by 36 kcal.

If a structural formula is to be a correct representation of a molecule, it must be consistent with the properties observed for that molecule. Here, then, is a property of benzene, its thermochemical stability, which does not appear to agree with that expected on the basis of either Kekulé structure.

In this same period, the 1920s, the notion of resonance was developing, and it was proposed that whenever it is not possible to write a single structural formula to account for all observed properties of a compound, several appropriate structures may be written, and the molecule is to be regarded as having no particular one of these structures but some weighted composite of them all. The molecule is spoken of as being a resonance hybrid of the several structures which may be written for it. However, the structures must be interconvertible by short electron shifts.

Accordingly, the actual structure of the aromatic ring is now regarded as a composite of the Kekulé structures and of a few more which must be included to account for spectroscopic properties. The resemblance of the actual structure of the benzene ring to the Kekulé forms is referred to as the Kekulé resonance of the ring. This resonance concept is not inconsistent with the ozonolysis experiments. The actual structure of *o*-xylene is something in between the two Kekulé structures, having an equal chance of reacting in either form. Therefore, half the time it reacts as if it had structure I, and the rest of the time as if it had structure II. This explains the ozonolysis products from *o*-xylene as previously described.

Furthermore, when the bond distances of the benzene ring were measured by X-ray diffraction techniques, instead of finding three with the C—C single bond distance and three with the C═C double bond distance, as the Kekulé structure would predict, all six carbon-carbon bonds were an identical distance between the normal single- and double-bond values. Moreover, in 1928 Raman[3] discovered a method for measuring the forces required to stretch or bend covalent bonds. These quantities are expressed in terms of *force constants*, and fall in different ranges for single, double, and triple bonds. When measured for the benzene nucleus, all six carbon-carbon bonds were found to have identical force constants rather than three in the single-bond range and three in the double-bond range as would be expected for a Kekulé structure. The bond distance and force constant results are exactly as expected from the resonance concept; a single structure with all carbon-carbon bonds being identical.

It must be kept clearly in mind that the concept of resonance does not imply that two types of *o*-xylene molecules are present, nor does it mean that half the time the molecules have structure I and half the time structure II. It means that *o*-xylene has a single, fixed structure which cannot be drawn. This structure is intermediate between I and II, and when *o*-xylene reacts, it has an equal chance of reacting in either form.

What has been said here about *o*-xylene applies to virtually all benzene derivatives, as well as many other types of compounds. To conserve time and space when writing the formula for benzene derivatives, only one Kekulé form is used. It is understood that either Kekulé form may be used, and that these are only symbols for the designated compounds, because the actual structures cannot be drawn. Furthermore, the CH's are usually omitted and a hexagon used.

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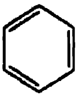
[3] C. V. Raman, Indian physicist, received the Nobel Award in physics in 1930. Cf. Section 6.4.



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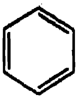
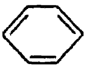
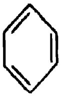
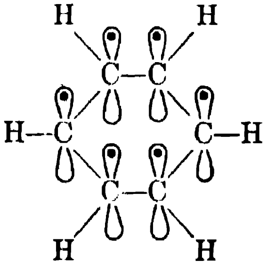
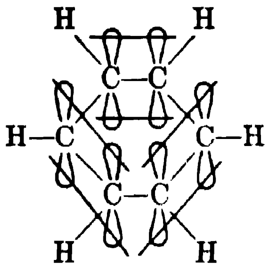


Through negligence, it is frequently drawn as a distorted hexagon, being either  or .

Up to here there has been a description of the benzene ring in terms of the resonance theory. Essentially the same picture may be given in terms of molecular orbitals. As in ethylene, each carbon atom of benzene uses three sp^2 hybrid orbitals, all coplanar, and leaving one p orbital at each carbon atom.



All atoms lie in the same plane and all p orbitals are perpendicular to this plane. Since any two adjacent p orbitals may coalesce to form π orbitals, two equivalent conditions could arise.



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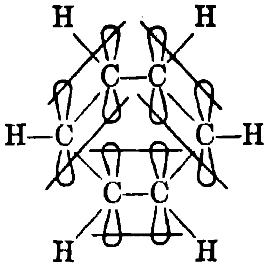
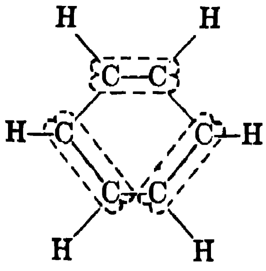
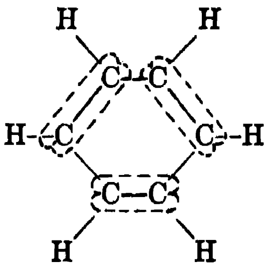
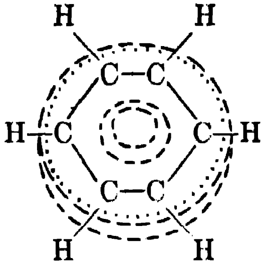






A more stable structure is one in which the six π electrons encompass all six carbon atoms in a molecular orbital surrounding the entire ring. This would look like two inflated inner tubes above and below the plane of the ring.



Thus, chemists think in terms of an electron cloud being above and below the plane of the benzene ring.

Two properties always associated with resonance molecules, i.e., molecules which are resonance hybrids of several forms, are *planarity* and *stability*. The molecules will be more stable than is expected on the basis of any single structural formula, and the atoms involved in the resonance system will lie in a single plane. For instance, the nonresonance molecule cyclohexane has a nonplanar chair conformation, whereas the benzene molecule is planar. Mention has already been made of the greater stability of the aromatic ring over that expected from bond energies for Kekulé or any other structural formulas.

The difference between the measured and the calculated heats of formation of a compound is called its resonance energy. Such values have been determined for many compounds, and a few are given in Table 7.4.

TABLE 7.4. RESONANCE ENERGIES OF SOME COMPOUNDS

Compound	*Resonance Energy (kcal/mole)*
Benzene	36
Biphenyl	72
Naphthalene	75
Anthracene	105
Styrene	51
Benzaldehyde	47
Phenol	50
Urea	41
1,3-Cyclohexadiene	1.8
1,3,5-Cycloheptatriene	6.7
Cyclooctatetraene	4.8

We have seen that structural formulas are used by chemists to represent the atomic framework of molecules. The formulas are based on the observed chemical and physical properties of compounds. As such, structural formulas (actually atomic models are used and structural formulas are merely projections of models on the plane of paper) facilitate chemists in communication regarding organic substances, the structures have enhanced an understanding and interpretation of organic reactions, and they aid in the prediction of new chemical reactions. An assigned structure can be used only as long as it is consistent with observed properties of a given molecule, and if a structure fails this condition it must be revised. We saw earlier in the chapter that this requirement even led to a revision of the structural theory of organic chemistry by incorporating the concept of resonance. Indeed, the study of the physical properties of molecules during the past several decades has brought about a considerable refinement of chemical theory and an amazing improvement in structure analysis.

7.3 USES OF BENZENE

Benzene is a strategically important chemical because it is used for the production of several other valuable substances. Over 300 million gallons are used annually, most of which comes from coal. The largest quantities of benzene go into the production of styrene, phenol, and nylon. Some of the important uses of benzene are given in Table 7.5 in order of their decreasing amounts.

TABLE 7.5. USES OF BENZENE

1. Styrene production	For synthesizing plastics and rubber
2. Phenol production	For making dyes, plastics, etc.
3. Nylon production	....
4. Aniline production	For dyes, drugs, etc.
5. Isopropylbenzene	Added to gasoline to raise octane rating
6. Detergents	Sodium dodecylbenzene sulfonates, nonionics, etc.
7. Insecticides	DDT, benzene hexachloride, *p*-dichlorobenzene
8. Maleic anhydride	Alkyd plastics, etc.
9. Solvent and misc.	....

7.4 COMMON AROMATIC REACTIONS

Four very common aromatic reactions will be given here for reference, but they will be discussed when the respective families of compounds are taken up. For conciseness, the symbol ϕ is often used to designate an aryl group, without regard to what substituents are present, just as R is used for aliphatic groups. Throughout the text, however, unless it is otherwise stated or obviously not so, general equations using R groups apply to aryl and alicyclic systems as well as aliphatic groups. It would be too cumbersome to illustrate each reaction for all three classes of compounds.

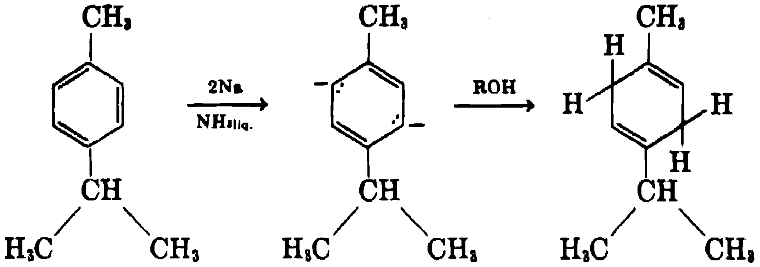
Halogenation: $\phi\text{—H} + X_2 \xrightarrow{Fe} \phi\text{—X} + HX$

Sulfonation: $\phi\text{—H} + HOSO_3H \rightarrow \phi\text{—}SO_3H + HOH$

Nitration: $\phi\text{—H} + HONO_2 \xrightarrow{H_2SO_4} \phi\text{—}NO_2 + HOH$

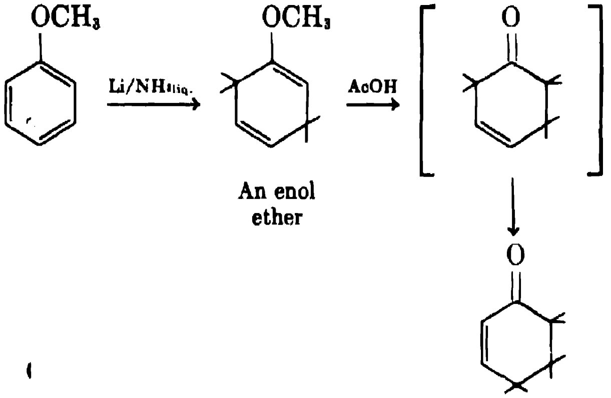
Alkylation: $\phi\text{—H} + RX \xrightarrow{AlCl_3} \phi\text{—R} + HX$

Birch reduction: Aromatic rings are reduced by lithium or sodium metal dissolved in liquid ammonia or amines to give 1,4-dihydro derivatives:



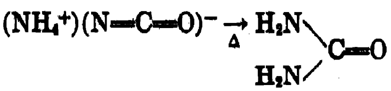
p-Cymene

γ-Terpinene



Brief historical development of organic chemistry. Although organic substances such as acetic acid, indigo, alcohol, tartar, sugar, resins, and oils, etc., had been known from biblical times and the Middle Ages, little was known about their chemistry until the beginning of the eighteenth century. Organic chemistry lagged behind inorganic chemistry because the reactions of organic substances were too complex to be understood and organic mixtures were too difficult to resolve. In 1675 Lemery published his famous *Cours de Chymie,* in which he classified compounds from natural sources as mineral, vegetable, or animal. It was more than a century later, 1780, that Bergmann first made a distinction between organic and inorganic substances, and in 1784 Lavoisier first showed that all compounds from vegetable and animal sources contain carbon and hydrogen and frequently nitrogen and phosphorus. The complexity of constitution and the combustibility of organic compounds led Berzelius to believe that they contained a "vital force" which put them beyond mortal synthesis from the elements, and in his *Lectures in Animal Chemistry,* first published in 1806, Berzelius wrote: "The part of physiology which describes the composition of living bodies, and the chemical processes which occur in them, is termed organic chemistry." In his textbook of 1827, Berzelius gave the first independent treatment of organic chemistry, and about this same period, Liebig gave the first university laboratory instruction in organic chemistry.

Until this time, largely as a result of Berzelius' influence, it was believed that organic substances were derived only from materials that were alive or had lived. All other substances such as salt, rock, sand, water, sulfur, etc., were classed as inorganic or nonliving. In 1828, Wöhler prepared, to his surprise, the organic compound urea from inorganic materials.



$$(NH_4^+)(N{=}C{=}O)^- \underset{\Delta}{\rightarrow} \begin{matrix}H_2N\diagdown\\ H_2N\diagup\end{matrix}C{=}O$$

Ammonium cyanate Urea

This experiment started the downfall of the vitalistic theory. Slowly, the leading contemporary chemists of that day recognized the significance of Wöhler's experiment. Then, in 1845, Kolbe was the first to prepare a naturally occurring organic compound from its elements, namely acetic acid. This led Gmelin, in 1848, to define organic chemistry as the chemistry of carbon-containing substances, and gradually the "vital force" doctrine was discarded. Now, of course, the study of the chemical reactions that take place in biological systems is termed *biochemistry*.

To trace the development of present-day views on chemical bonding, one must go back to the early nineteenth century. In trying to carry over to organic compounds, certain notions held in that period concerning inorganic substances, Berzelius proposed his electrochemical or *dualistic theory*, in which the formation of a compound was due to the uniting of an electronegative substance (oxygen or an acid) with an electropositive substance (usually a metal or a base). This dualistic theory failed when applied to organic compounds, so that the recognition in 1832 by Liebig and Wöhler, that certain organic radicals or atomic groupings could be traced unchanged through a series of reactions, gave new impetus to work in organic chemistry. When Dumas showed in 1834 that the electronegative element chlorine could replace the electropositive element hydrogen in wax, he proposed a theory of types, which was developed by Laurent and Gerhardt. In this theory, compounds were related to fundamental inorganic types, hydrogen, hydrogen chloride, water, and ammonia, from which the organic compounds could be obtained by substituting organic radicals for hydrogen. For illustration, according to this theory, there are the four types:

$$\begin{array}{cccc} \textit{Hydrogen Type} & \textit{Hydrogen Chloride Type} & \textit{Water Type} & \textit{Ammonia Type}\\ \left.\begin{matrix}H\\H\end{matrix}\right\} & \left.\begin{matrix}H\\Cl\end{matrix}\right\} & \left.\begin{matrix}H\\H\end{matrix}\right\}O & \left.\begin{matrix}H\\H\\H\end{matrix}\right\}N \end{array}$$

in which one could make simple substitutions of the ethyl radical.

$$\begin{array}{cccc} \left.\begin{matrix}C_2H_5\\H\end{matrix}\right\} & \left.\begin{matrix}C_2H_5\\Cl\end{matrix}\right\} & \left.\begin{matrix}C_2H_5\\H\end{matrix}\right\}O & \left.\begin{matrix}C_2H_5\\H\\H\end{matrix}\right\}N \end{array}$$

For Williamson's preparation of ether in 1850, one could write,

$$\left.\begin{matrix}C_2H_5\\K\end{matrix}\right\}O + \left.\begin{matrix}C_2H_5\\I\end{matrix}\right\} \longrightarrow \left.\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\right\}O + KI$$

However, these early theories did not consider the arrangements of atoms in the organic radicals. In 1852 Sir Edward Franklin first expressed the concept of what is now called *valence*, and in 1858 Kekulé published in Liebig's *Annalen* his famous definitive paper on the chemical bonding of carbon. He stated that carbon is quadrivalent and can form bonds with other carbon atoms, thereby losing part of its capacity to unite with other elements, and that carbon atoms can form open chains as well as closed rings. In that same year, Kekulé and Couper independently introduced the idea of valence bonds and the pictorial representation of molecules.[4] Couper's formulas were less bulky and easier to draw than were Kekulé's. In 1861, Butlerov first used the term *chemical structure* in a paper read before a scientific congress in Germany, in which he emphasized that each organic compound has a fixed, real structure which determines its properties. Herein are the foundations for the present-day practice of employing graphic formulas for representing molecules, and of interpreting their properties in terms of these structural formulas. Although several persons contributed ideas leading up to this conception, notably Berzelius, Dumas, Liebig, Laurent, Gerhardt, Kolbe, and Franklin, it was really Kekulé, Couper, and Butlerov who clearly outlined the framework which provided the backbone for the entire field of organic chemistry. Then, in 1865, Kekulé made what has been considered his greatest contribution to organic chemistry, and that was his proposal for the structure of benzene. Although our present-day concept is somewhat different, Kekulé's novel idea started organic chemists to thinking along entirely new avenues which brought about a rapid development of organic chemistry.

In 1863 Geuther discovered the tautomerism of ethyl acetoacetate, in 1876 Butlerov gave the first explicit definition of the phenomenon of tautomerism, and in 1885 the term *tautomerism* was proposed by Laar. Although isomerism had been recognized earlier, and Berzelius had suggested the term *isomerism* in 1810, Wislicenus in 1863 first attributed the phenomenon to differences in spatial arrangements of atoms within molecules. Then, LeBel, in 1874, and van't Hoff, in 1875, independently resolved the problem of optical isomerism on the basis that the four valences of carbon form a tetrahedron.

Following Thompson's discovery of the electron (1897), and Lord Rutherford's proposal of a planetary, particle structure of atoms (1911), Kossel and Lewis independently proposed their electronic theories of valence (1916). Lewis also suggested the occurrence of electron-pair bonds. In the same period, Bohr gave his quantum theory of the atom, and somewhat later there came an embryonic notion of resonance from the work of Heisenberg. This led to the concepts of atomic and molecular orbitals, orbital hybridization, and finally to intermolecular coordinate covalent bonds (cf. Chapter 19).

Shortly after the birth of resonance theory, fostered largely by L. Pauling, organic chemistry grew rapidly along two lines. One is commonly called *natural products chemistry* and is concerned with the determination of structure and synthesis of complex compounds resembling those of natural origin. Britain's Sir Robert Robinson (Nobel Prize in 1947) and Switzerland's L. Ruzicka (Nobel Prize in 1939) and P. Karrer (Nobel Prize in 1937) were particularly active during the early stages of the expansion of natural products chemistry. The other arm of organic chemistry is referred to as *physical organic chemistry* in which the charge distribution of unreacting and reacting molecules and the mechanisms of reactions are studied. Sir Christopher Ingold of England is the principal forefather of this phase of organic chemistry. In recent years, however, these two arms of organic chemistry have become folded to supplement each other. Physical organic chemistry has facilitated the synthesis, analysis, and structure determination of many complex molecules, whereas natural products chemistry has provided fruitful examples for the development of ideas and methods in physical organic chemistry.

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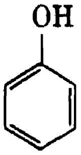
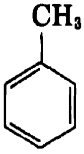
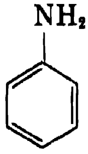
[4] William Higgins, in 1789, was the first to publish diagrammatic formulas, but his intent was somewhat different from what it is today.

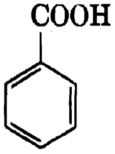
7.5 NOMENCLATURE OF BENZENE DERIVATIVES

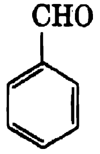
Many benzene derivatives have trivial names, such as phenol for hydroxybenzene. These will have to be learned as they are encountered. For a start, a few very common ones are given here.


Phenol

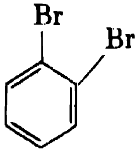

Toluene

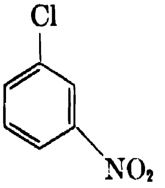

Aniline

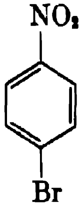

Benzoic acid


Benzaldehyde

When two substituents are attached to the benzene ring, they may be situated on adjacent, alternate, or opposite carbon atoms. These positions are referred to as *ortho*, *meta*, or *para*, respectively, and are abbreviated *o*, *m*, or *p*.

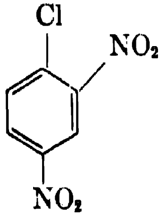

ortho-Dibromobenzene

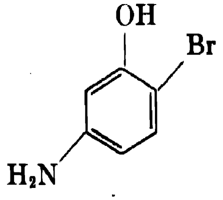

meta-Nitrochlorobenzene

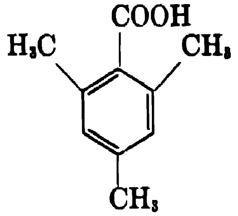

para-Bromonitrobenzene

Either substituent may be named first.

When there are more than two substituents, the relative positions are indicated by numbers.


2,4-Dinitrochlorobenzene


2-Bromo-5-aminophenol

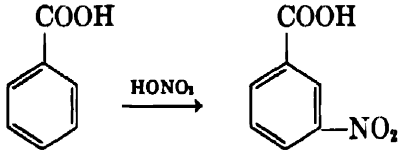

2,4,6-Trimethylbenzoic acid (mesitoic acid)

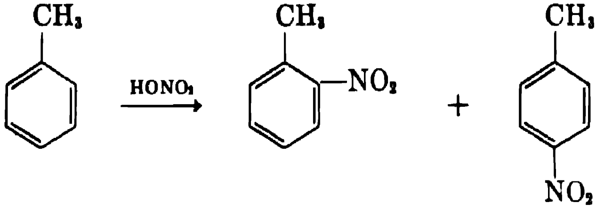
The group named last, or the functional group, is regarded as having the 1-position. Numbering may be done clockwise or counterclockwise, although it will most often be the former.

7.6 ORIENTATION OF AROMATIC SUBSTITUTION

Reagents reacting with aromatic compounds may be nucleophilic, electrophilic, or free radicals. Most common reactions are with electrophilic reagents; hence, this section is limited to electrophilic substitution—that is, the reagents are electron-seeking, and therefore, other things being equal, they will tend to react with the carbon atom of the ring which most readily provides electrons.

For many years, chemists have been fascinated by the fact that substitution reactions with monosubstituted benzenes yield varying amounts of *ortho*, *meta*, and *para* isomeric disubstitution products. It was early recognized that groups may be classified as chiefly *ortho*- and *para*-directing, or *meta*-orienting. For instance, upon nitrating benzoic acid, the incoming nitro group takes a position *meta* to the carboxyl group, but in the nitration of toluene, the nitro group enters *ortho* and *para* to the methyl group.





Chemists have devoted considerable work to determining the preferential orienting effects of groups, and the percentages of *ortho*-, *meta*-, and *para*-substitution occurring in the mononitration of various monosubstituted benzenes are given in Table 7.6. The substituents are listed in order of increasing *meta*-directing effect.

It can be seen in Table 7.6 that only a very few groups lead to all *ortho*- and *para*-substitution, or all *meta*-substitution. There is a complete gradation from one extreme to the other. Hence, the classification of groups into *o,p*-directing, or *m*-directing types merely refers to their principal directing influence.[6] The statistical distribution to be expected in the absence of any directive influence is that listed for H. Therefore, any substituent that leads to more than 40 per cent *meta* isomer is classified as a *m*-directing group.

The orientation observed in reactions with monosubstituted benzenes depends chiefly upon the nature of the substituent. However, other factors help to control the position taken by an entering group relative to a substituent already present. Of these second-order factors, the characteristics of the entering group are very important. One such factor is the spatial size of the entering group. For illustration, the orientation for monoalkylation of toluene is given in Table 7.7. It is shown there that, as the size of the entering group

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[6] For example, the major product in the nitration of benzaldehyde is *m*-nitrobenzaldehyde, but there is sufficient *o*-isomer produced as a side-product to make this an economical process for the production of *o*-nitrobenzaldehyde.

TABLE 7.6. DISTRIBUTION OF MONONITRATION PRODUCTS FROM MONOSUBSTITUTED BENZENES

Substituent	% *Ortho*	% *Meta*	% *Para*
$-OH$	40	—	60
$-F$	12	0.5	87
$-Cl$	29.6	0.9	69.5
$-Br$	36.5	1.2	62.3
$-I$	37.9	2.1	60
$-CH_3$	58.5	4.4	37.1
$-CH_2CH_3$	43	6.5	48.5
$-CH(CH_3)_2$	30	7.7	62.3
$-C(CH_3)_3$	15.8	11.5	72.7
$-CH_2CO_2Et$	42	10.6	47.4
$-CH_2Cl$	32	15.5	52.5
$-CH_2F$	28	18	54
$-CHCl_2$	23.3	33.8	42.9
$-H$	(40)	(40)	(20)
$-Si(CH_3)_3$	26.6	41.7	31.6
$-CCl_3$	6.8	64.5	28.7
$-CO_2Et$	24	72	4
$-CO_2H$	18.5	80.2	1.3
$-CN$	17	81	(2)
$-CH_2\overset{+}{N}(CH_3)_3$	—	85	15
$-\overset{+}{N}(CH_3)_3$	—	89	11
$-NO_2$	6.4	93.3	0.3
$-CF_3$	—	99	—

increases, the amount of *ortho* isomer obtained decreases. This is due to the spatial barrier preventing the reagent from approaching the substituent for *ortho*-substitution. A smaller steric effect also may occur for the substituent, as shown in Table 7.8. Here again, as the size of the alkyl group increases, less *ortho*-substitution takes place.

Also, the nature of the reagent affects the orientation observed. For instance, halogenation of toluene gives less than 1 per cent *meta*-substitution,

TABLE 7.7. ORIENTATION IN MONOALKYLATION OF TOLUENE

Entering Group	% *Ortho*-substitution	% *Meta*-substitution	% *Para*-substitution
$-CH_3$	53.8	17.3	28.8
$-CH_2CH_3$	45	30	25
$-CH(CH_3)_2$	37.5	29.8	32.7
$-C(CH_3)_3$	0	7	93

TABLE 7.8. ORIENTATION IN MONONITRATION OF ALKYLBENZENES

Compound	% *Ortho*-substitution	% *Meta*-substitution	% *Para*-substitution
$C_6H_5CH_3$	58.5	4.4	37.1
$C_6H_5CH_2CH_3$	45	6.5	48.5
$C_6H_5CH(CH_3)_2$	30	7.7	62.3
$C_6H_5C(CH_3)_3$	15.8	11.5	72.7

nitration gives 4 per cent, and alkylation gives up to 30 per cent *meta*-substitution.

It can be seen, then, that these second-order effects have a significant influence upon orientation, but they do not change a substituent from one class of orienting group to the other. Hence, a group that directs the second entering group to the *ortho* and *para* positions in nitration will also direct chiefly to these positions in alkylation, bromination, sulfonation, and other electrophilic reactions. Many empirical rules have been proposed by which a chemist may predict the major orienting property of substituents.[6] These rules have been based upon various physical properties of the substituents and also upon their constituent atoms. Each has some merit, but each fails in one or more cases. Nevertheless, they are useful guides in planning syntheses, as well as for predicting the physical properties of substituted benzenes. Probably the easiest rule to learn and the most general one is the following:

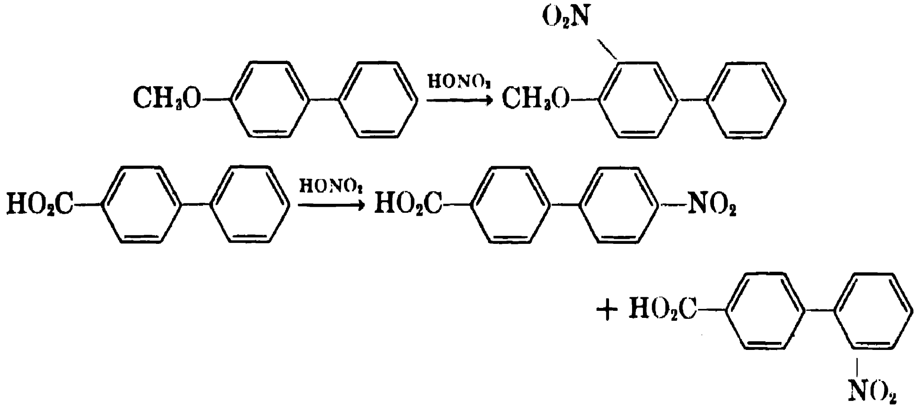
Groups attached by atoms forming only single bonds are o,p-directing.
Exceptions: $—CX_3$, $—NR_3^+$ (which are *m*-orienting).
Groups attached by atoms forming multiple bonds are m-directing.
Exceptions: $—C_6H_5$, $—CH{=}CH_2$ (which are *o,p*-directing).

For example, —OH, $—NH_2$, —OR, $—NR_2$, $—CH_3$, and —X (the halogens) are *o,p*-directing, while —CHO, —COOR, —CN, $—SO_3H$, and $—NO_2$ are *m*-orienting. Note that it is the atom attached to the ring which is the key atom for applying this rule. Thus, $—CH_2COOH$, $—CH_2NO_2$, and $—CH_2—CH{=}CH_2$ are *o,p*-directing, although there are multiple bonds in the groups, because the atom attached to the ring in each case forms only single bonds.

Classification of groups into two classes has also been very convenient for other purposes. It is found that the chemical and physical properties of aromatic compounds depend upon the nature of the ring substituents. For instance, the color, dipole moments, absorption characteristics of ultraviolet and infrared light energy, and other physical properties of substituted benzenes can be accounted for on a basis of the substituents present. It is observed that *m*-orienting groups deactivate the ring, and *o,p*-directing groups activate the ring. The more exclusively *m*-orienting the group is, the more ring-

[6] L. N. Ferguson, *Chem. Reviews* **50**, 47 (1952).

deactivating it is. If there are two benzene rings joined together and one ring has a substituent, the class of the substituent will determine in which ring further substitution will take place.



The methoxyl group, being *o,p*-directing, activates the attached ring, thereby facilitating reaction with that ring. The carboxyl group is *m*-orienting and ring-deactivating; therefore, reaction occurs with the other ring. The effect of the substituent upon ring activity is important, and it is to be remembered that:

Strong reactions, such as sulfonation and nitration, give good yields with all substituents, including *m*-orienting groups.

Weak reactions, such as alkylation, give very poor yields with *m*-orienting substituents present, although they go well with *o,p*-directing groups present.

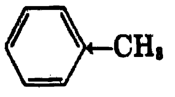
Thus, one does not attempt to alkylate nitrobenzene. The halogens are unusual in that they are *o,p*-directing but ring-deactivating.

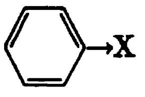
It is also found that *m*-orienting groups, when *ortho* or *para* to halogen atoms, OH groups, or NH_2 groups, will

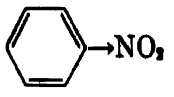
1. Activate the halogen
2. Increase the acid strength of the OH group
3. Diminish the base strength of the NH_2 group.

These effects will be pointed out when the respective families of compounds are taken up.

These orientation effects of substituents, as well as the physical and chemical properties of aromatic compounds, can be explained fairly well in terms of induction, resonance, and steric requirements. For illustration, the orienting effect and effect of substituents on ring reactivity are primarily the result of the polar nature of the substituent. Through induction or resonance, or both, groups decrease or increase the over-all electron density of the ring, and also about specific carbons of the ring. The higher the electron density, the greater is the rate of reaction with electrophilic reagents. Thus, because of relative group electronegativities, the methyl group increases the electron density of the ring through induction, while halogens and the nitro group decrease the over-all electron density of the ring.

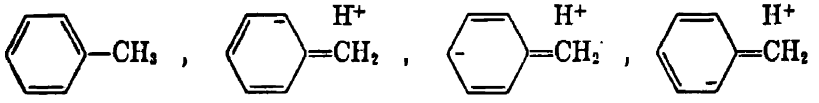


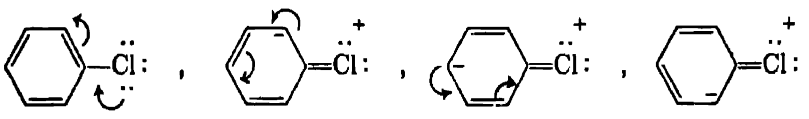


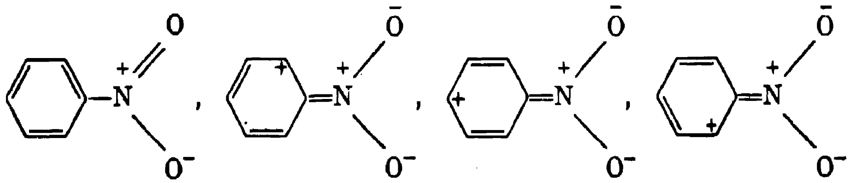


Accordingly, toluene reacts faster than benzene, but halobenzenes and nitrobenzene react slower. In other words, alkyl groups are ring-activating, and halogens and the NO_2 group are ring-deactivating.

At the same time, the hyperconjugation (resonance involving single bonds) of toluene, and the resonance of halobenzenes and nitrobenzene affect the relative electron densities of the *ortho*, *meta*, and *para* carbon atoms of the ring.







The curved arrows indicate the electron migrations which would give the next structure. According to these structures, the *ortho* and *para* positions in toluene and chlorobenzene have a higher electron density (greater negative charge) than the *meta* positions, and hence, substitution takes place preferentially at the *ortho* and *para* positions. The electron density at the *ortho* and *para* positions of nitrobenzene are lower than at the *meta* positions, so substitution takes place at the *meta* positions.

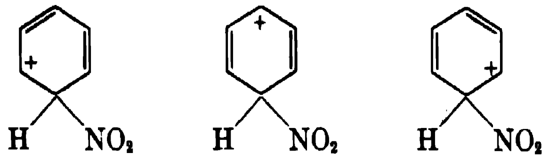
Electrophilic aromatic substitution has a strong ionic character. For example, nitration with the usual HNO_3—H_2SO_4 mixtures takes place as follows:

$$2H_2SO_4 + HONO_2 \rightleftharpoons 2HSO_4^- + H_3O^+ + {}^+NO_2 \qquad (1)$$

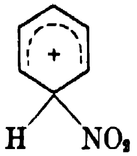
$$ArH + {}^+NO_2 \xrightarrow{\text{slow}} \overset{+}{A}rHNO_2 \qquad (2)$$

$$\overset{+}{A}rHNO_2 \longrightarrow ArNO_2 + H^+ \qquad (3)$$

where ArH is an aromatic compound and ArHNO_2 is a resonance hybrid of forms such as



This resonance hybrid is frequently drawn as

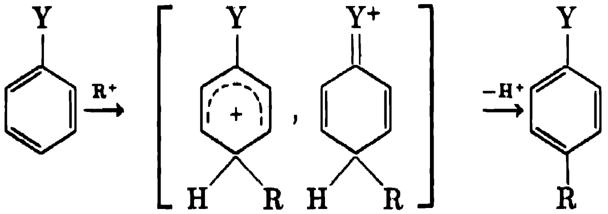


in which the dotted line represents partial bonds of the delocalized π electrons. Nitric acid in concentrated sulfuric acid is completely ionized as shown in equation (1). Thus, the sulfuric acid solutions have essentially no vapor pressure, i.e., nonvolatile substances are present, and the conductivities indicate four ions are in solution. Also, the nitronium ion has been identified in these solutions by Raman spectroscopy. Nitration rates parallel the concentration of nitronium ion. In nitric acid alone, the concentration of $\overset{+}{N}O_2$ ion is small, and nitrations are therefore slow in this medium except with highly reactive aromatic rings.

Alkylation generally proceeds via an ionic mechanism:

$$R{-}X + AlX_3 \rightleftharpoons R^+ + {}^-AlX_4 \qquad (4)$$

Mixture has a small conductivity



(5)

In this example, Y is an *o,p*-directing group. Mixtures of an arene, an alkyl halide, and AlX_3 have a high conductivity, which confirms the ionic character of this reaction.

Halogenation may take place by a mechanism analogous to nitration, in which a halogenonium ion, X^+, is first formed and attacks the aromatic ring, or via the initial formation of a charge-transfer complex (cf. page 469):

$$ArH + X_2 \rightleftharpoons ArH:X_2 \qquad (6)$$

$$\begin{tikzcd} ArH:X_2 \arrow[r, "C", "slow"'] & \overset{+}{H}ArX + {}^{-}CX \arrow[d, "-H^+"] \\ & ArX \end{tikzcd} \tag{7}$$

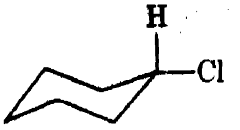
C is a catalyst such as FeX_3, AlX_3, Ag^+, or even another halogen molecule.

A description of polar effects, as was given above for CH_3, X, and NO_2, can be given for other substituents. In some molecules, the effects of resonance and induction operate to supplement each other, and in other molecules these effects oppose each other. In addition to the polar nature of the substituents, orientation is influenced by the polar effect of the reagent, by steric requirements of the substituent and reagent, and by the nature of the solvent. These second-order effects were illustrated in the text above. However, the polar nature of the substituent largely determines whether it is *o,p*-directing or *m*-orienting. Its polar character is also chiefly responsible for the physical properties of substituted benzenes. For instance, the dipole moments and absorption spectra may be accounted for in terms of the polar natures of substituents.

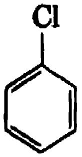
A molecular orbital of π electrons about a multiple bond or a conjugated system of multiple bonds may be regarded as a tube of moving electrons along the framework of conjugated atoms. The charge-density varies along the tube depending upon the type of atoms along the atom-chain. This charge-density can be computed sometimes by theoretical methods. Resonance theory has provided an alternative way of indicating the charge-densities of π-electrons in terms of structural formulas. There are several principles that serve as guides in writing resonance structures and for assessing their relative importance. The more important rules are the following:

(i) *Resonance structures are interconvertible by one or a series of short electron-shifts.*
(ii) *Resonating structures must have the same number of unpaired electrons.*
(iii) *The more covalent bonds there are in a structure, the greater is its stability and the greater is its contribution to the resonance hybrid.*
(iv) *Dipolar structures are less stable than nonpolar structures.*
(v) *The more nearly equal in stability are resonance structures, the greater is the degree of resonance.*

An approximate structural formula can normally be written for a compound based on its chemical and physical properties. Other structures can then be derived from the first structure as are needed to be consistent with all observed properties. For illustration, the structures of chlorocyclohexane and chlorobenzene are given as I and II. Structure I is consistent with all properties

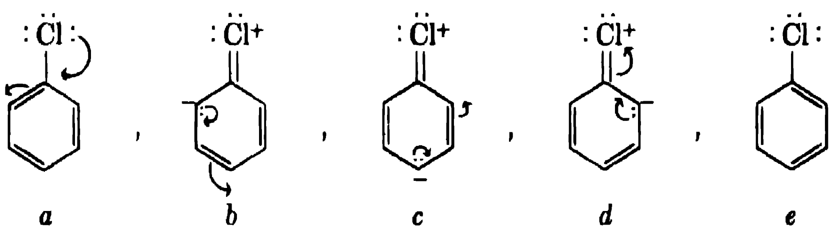


I



II

observed for chlorocyclohexane. However, in order to account for the shorter C—Cl bond length in chlorobenzene (1.69 Å, in comparison to 1.78 Å in alkyl chlorides), for the resistance to nucleophilic substitution, for the smaller dipole moment of chlorobenzene than of alkyl chlorides, for the ortho-para orientation, and for other properties of chlorobenzene, its actual structure is regarded as a resonance hybrid of structures II*a*–II*e*, with II*a* and II*e* making the major contribution.



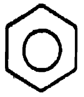
II

Each structure is derived from the others by short electron-shifts involving π and lone-pair electrons.

7.7 AROMATIC CHARACTER OF RING STRUCTURES

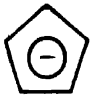
In Section 7.2 it was pointed out that the H/C ratios of benzene and its derivatives indicate that the benzene ring must form multiple bonds but the ring does not exhibit typical olefinic properties such as rapid oxidation, polymerization, and addition reactions. This chemical inertness was defined as *aromatic character*. It was also shown that the ring has an unexpected thermochemical stability expressed as its resonance energy. One may wish to identify aromatic character by this large resonance energy. The resonance energy of cyclooctatetraene for instance, is only 4.8 kcal/mole and that of 1,3-cyclohexadiene is 1.8 kcal, whereas that of benzene is 36 kcal. Accordingly, in recent years there has been a trend towards defining aromatic character in terms of the unusually large stability which accompanies a *planar*, completely conjugated ring system. Often low chemical reactivity (the classical definition) and large resonance energy occur together, which is the case for benzene. We shall see below, however, that some compounds are aromatic according to the modern definition but not by the classical definition.

In 1931 Hückel of Germany made a remarkable prediction, based on theoretical chemistry, that there will be a large resonance energy associated with a conjugated ring system having $(4n + 2)$ π electrons, where n is an integer. Three ring structures for which $n = 1$ are C_6H_6, $C_5H_5^-$, and $C_7H_7^+$.



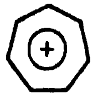
C_6H_6

Benzene



$C_5H_5^-$

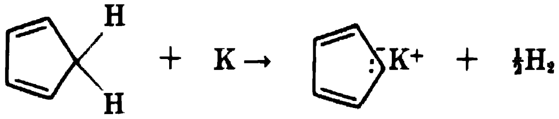
Cyclopentadienyl anion



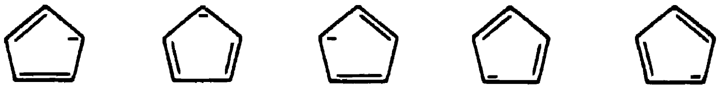
$C_7H_7^+$

Tropylium cation

Each ring has six π electrons. The cyclopentadienyl anion can be easily prepared by reacting cyclopentadiene with an alkali metal:



The anion may be regarded as a resonance hybrid of five equivalent structures:

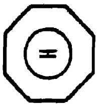


Hence, with the symbolism used for benzene, the dotted line or circle is written in the ring to express the equivalency of the carbon-carbon bonds of an aromatic ring. The tropylium cation is a resonance hybrid of seven equivalent structures in which the positive charge resides equally on each of the seven carbon atoms.

Each of these three rings is planar and has an evenly distributed electron cloud around the ring, which gives them aromatic character in the classical and modern sense. Thus, it is found for each, that

1. All C—C bonds of the ring are equal in length, between the typical aliphatic C—C and C═C bond lengths.
2. The ring has a large resonance energy.
3. The ring undergoes substitution rather than addition reactions.
4. The ring resists hydrogenation.
5. The ring does not undergo the Diels-Alder reaction.

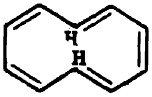
Another physical measurement which can be used to identify an aromatic ring is n.m.r. spectroscopy. The electron cloud over the carbon frame of an aromatic ring acts as a circular current, called a ring current, and it produces a certain magnetic effect upon the protons attached to the ring. This shows up in the chemical shift values for "aromatic protons" for which $\tau = 1\text{–}3$ (an arbitrary unit for chemical shifts) whereas τ is larger for nonaromatic protons. For example, $\tau = 2.5$ for benzene protons and 4.31 for cyclooctatetraene protons. Although the latter compound has a completely alternating ring of C—C and C═C bonds, it is not aromatic because no two adjacent C═C bonds are coplanar and therefore there is little resonance or π-electron delocalization around the ring. In contrast, cyclooctatetraene has been reduced with potassium metal to give the dianion, structure III. This ion is found to be planar, and all carbon-carbon bonds are equivalent. Notice that III conforms to Hückel's rule in which $n = 2$ (10 π electrons), whereas cyclooctatetraene does not (8 π electrons).



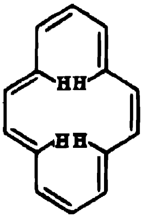
III

Cyclooctatetraene
dianion

Similarly, [10]annulene and [14]annulene are not aromatic according to

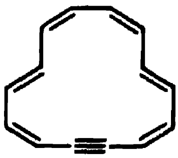


[10]Annulene



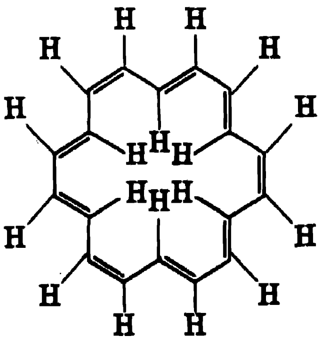
[14]Annulene

either the classical or the modern definition. Thus, [14]annulene does not undergo substitution reactions nor does the ring sustain an induced ring current. This can be attributed to their nonplanar structures owing to the crowded intraannular protons. This prevents [14]annulene, for example, from forming stable charge-transfer complexes (cf. Section 19.1). On the other hand, dehydro[14]annulene, structure IV, and [18]annulene, structure V, are aromatic on the basis that their n.m.r. spectra show that they sustain an induced



Dehydro[14]annulene

IV

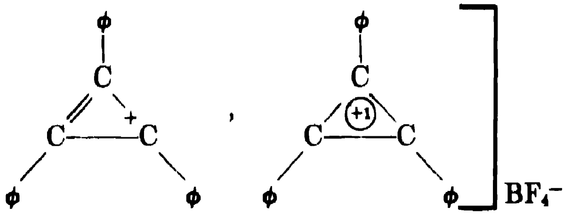


[18]Annulene

V

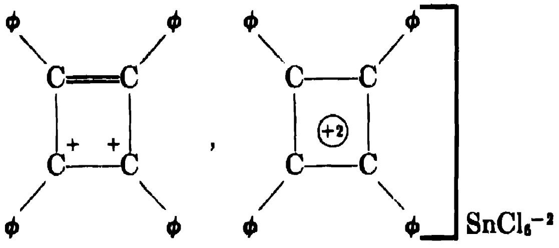
ring current.[7] For instance, V has two peaks in its n.m.r. spectrum, one in the aromatic range at 1.1 τ for the 12 peripheral protons and another of half this intensity at 11.8 τ for the six intraannular protons. Compound IV has been shown to undergo aromatic nitration, acylation, and sulfonation. It forms crystalline charge-transfer compounds but, it does not undergo the Diels-Alder reaction.

Two examples of an aromatic ring with 2 π electrons, i.e., $n = 0$ in $(4n + 2)$ π electrons, are the triphenylcyclopropenium cation VI and the tetraphenylcyclobutenium dication VII.



VI

Triphenylcyclopropenium borofluoride

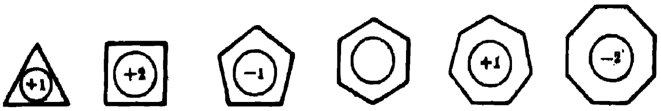


VII

Tetraphenylcyclobutenium hexachlorostannate

The carbon atoms in each ring of VI and VII are equivalent in terms of electron density and covalent radii.

We see, then, among the simple aromatic rings there are the following:



Number of π electrons = 2 2 6 6 6 10

STUDY EXERCISES

1. Write general equations for the nitration, sulfonation, halogenation, and alkylation of toluene.

2. What structures were proposed for benzene by Dewar, Thiele, Kekulé, and Ladenburg, and why was each structure abandoned?

---

[7] Y. Gaoni and F. Sondheimer, *J. Am. Chem. Soc.*, **86**, 521 (1964).

3. What is the present concept of the structure of the aromatic nucleus, and what evidence is there for this viewpoint?

4. State an empirical rule by which one may predict the position taken by a second entering group in an electrophilic reaction with a monosubstituted benzene.

5. Name several chemicals obtained from coal tar.

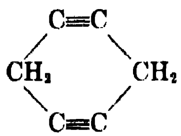
6. Cite evidence for the statement that *m*-orienting groups deactivate the ring.

7. What is believed to be the source of coal?

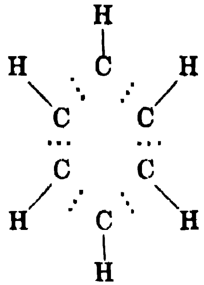
8. What are monosubstituted benzenes with the following substituents called: —COOH, —CHO, —OH, $—NH_2$, $—CH_3$?

9. What properties would exclude the following structures for benzene: (a) $CH_2{=}CH{-}CH{=}CH{-}CH{\equiv}CH$;

(b)

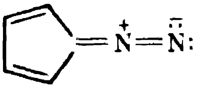


(c)



10. Predict the product of the reaction between propylene and benzene in the presence of HF.

11. Diazocyclopentadiene appears not to undergo the Diels-Alder reaction and can be nitrated to give two isomeric mononitro substitution products. How do you explain these observations?



12. How do the shapes of a naphthalene and a *trans*-decalin molecule compare?

TEST QUESTIONS, Set 7

1. Starting with benzene, how could you prepare *m*-nitrochlorobenzene, *p*-nitrobromobenzene, and *p*-nitrotoluene in the laboratory?

2. How could cyclohexene be distinguished from benzene by qualitative test tube experiments?

3. A 12.3-gram sample of a liquid mixture of cyclohexene and benzene was treated with 1 *M* $KMnO_4$ in cold, aqueous Na_2CO_3, and 20 ml of the oxidant were reduced. If it is assumed that the cyclohexene was oxidized to cyclohexanediol, what was the percentage of cyclohexene in the mixture?

4. What would be the molar ratio of products from the ozonolysis and hydrolysis of the resulting triozonide from *m*-ethyltoluene?

5. How many nuclear monobromination products are possible from (a) *o*-xylene; (b) *m*-xylene; (c) *p*-xylene? How could one distinguish the three isomers of xylene on a basis of your answer?

6. What should be the heat of formation of toluene if it had a Kekulé structure?

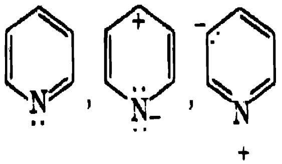
7. Why should a nitro group para to a halogen atom facilitate hydrolysis of the halogen atom?

8. A compound X, C_7H_7Br, prepared from 1,3,5-cycloheptatriene, is soluble in water but insoluble in nonpolar solvents, and aqueous solutions give an immediate precipitate of AgBr when aqueous silver nitrate is added. Reduction of X yields cycloheptane. Propose a structure for X and give the basis of your answer.

9. A hydrocarbon R, C_9H_8, rapidly decolorizes cold aqueous permanganate and

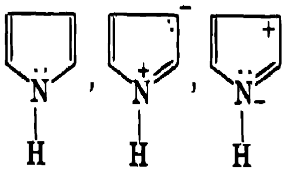
readily absorbs one mole of hydrogen. Vigorous hydrogenation of C_9H_8 gives a compound of formula C_9H_{16}. Strong oxidation of R yields phthalic acid. Propose a structure for R and give the basis for your answer.

10. The *c* structures among the following make little or no contribution to the respective resonance hybrids. Give a reason for this and show how structures *b* and *c* are derived from *a* in each case:



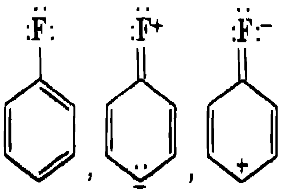
a *b* *c*

Pyridine



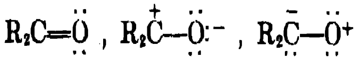
a *b* *c*

Pyrrole



a *b* *c*

Fluorobenzene



$R_2C=\ddot{O}$, $R_2\overset{+}{C}-\ddot{O}:^-$, $R_2\overset{-}{C}-\ddot{O}^+$

a *b* *c*

A ketone

8

Arenes
(Aromatic hydrocarbons)

The term *arene* has been approved by the American Chemical Society Nomenclature, Spelling, and Pronunciation Committee to mean an aromatic hydrocarbon. The alkylbenzenes will be taken up first; then other aromatic systems will be discussed briefly.

8.1 PREPARATION OF ALKYLBENZENES

Alkylbenzenes are commonly prepared in the laboratory by alkylating benzene through one of two reactions.

Friedel-Crafts reaction:

$$\phi\text{—H} + \text{RX} \xrightarrow{\text{AlCl}_3} \phi\text{—R} + \text{HX}$$

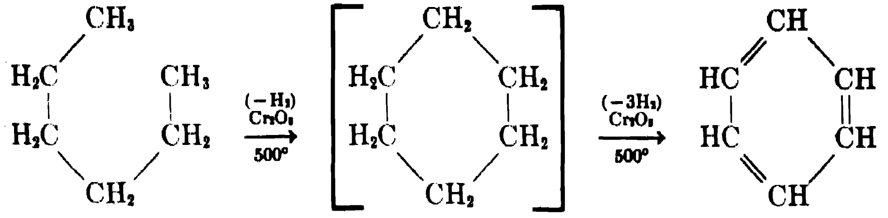
This reaction is weak and gives little or no yield with *m*-orienting groups in the ring. Yields are good in the presence of *o,p*-directing groups. It requires an acid catalyst mole for mole with the alkyl halide. Aluminum chloride is the most common catalyst, although other agents, such as $ZnCl_2$, FeX_3, and $SnCl_4$, have been used. These substances are often referred to as *Friedel-Crafts-type catalysts*. In this reaction, the halogen must come from the alkyl halide (or acyl halide for acylation as shown on page 315).

Wurtz-Fittig reaction:

$$\phi\text{—X} + \text{R—X} + 2\text{Na} \rightarrow \phi\text{—R} + 2\text{NaX}$$

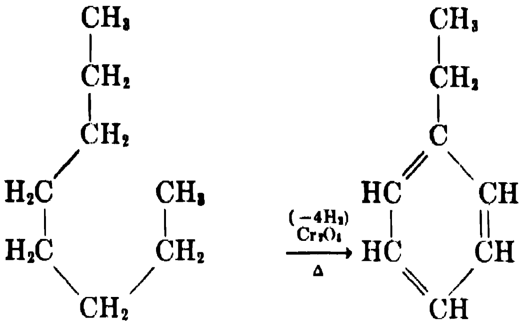
In 1855 Wurtz developed the reaction for uniting two alkyl groups in the presence of sodium metal, and in 1864 Fittig used the method for attaching an alkyl group to an aryl group. The Wurtz reaction is seldom used with two different alkyl groups, for then three products result which may not be separated easily. However, the Wurtz-Fittig reaction gives predominantly the alkylbenzene, because sodium reacts faster with the alkyl halide to yield alkylsodium, RNa. This, in turn, reacts faster with the aryl halide to give an alkylbenzene.

Alkylbenzenes may be produced by large-scale applications of the Friedel-Crafts or Wurtz-Fittig reactions. A few alkylbenzenes are obtained also from coal tar and the aromatization process. This latter reaction involves cyclization and dehydrogenation of *n*-alkanes.

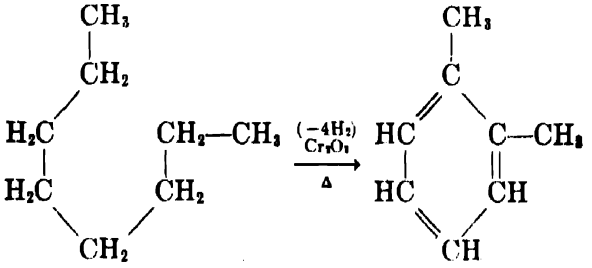


n-Hexane Benzene

Toluene is obtained in a high yield from *n*-heptane. *n*-Octane gives *o*-xylene and ethylbenzene.

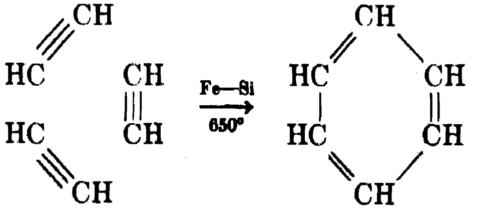


n-Octane Ethylbenzene



n-Octane *o*-Xylene

In Germany, more so than in the United States, benzene is produced by the trimerization of acetylene.



Benzene could be produced in the laboratory by decarboxylation of benzoic acid, but this would merely be a laboratory exercise and of no practical significance. The aromatization process was known for many years, but the war and postwar demands on benzene and these alkylbenzenes for plastics, synthetic rubber, textiles, explosives, and high-octane gasoline forced the development of this process as a means of supplementing the supply obtained from coal tar.

8.2 PROPERTIES OF ALKYLBENZENES

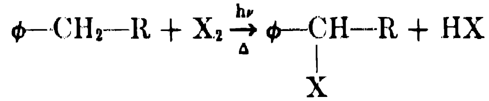
The physical properties of alkylbenzenes are essentially like those of benzene. Many alkylbenzenes are liquids. Arenes are practically insoluble in water, acids, and aqueous alkali. They have a measurable solubility in aqueous silver nitrate owing to the formation of complexes (Section 19.1).

The alkyl group is *o,p*-directing and mildly ring-activating. Alkylbenzenes, therefore, undergo the general nuclear reactions, such as nitration, halogenation, and alkylation, more readily than does benzene. Substances may also react with the alkyl groups. The side chain has aliphatic properties and is therefore halogenated under the same conditions as alkanes, namely, with illumination and thermal catalysis, or sulfuryl chloride plus peroxide.

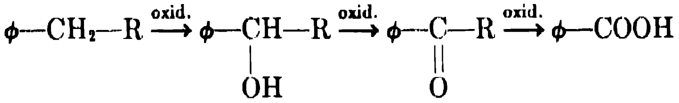
$$\phi\text{—CH}_3 + \text{X}_2 \xrightarrow[\Delta]{h\nu} \phi\text{—CH}_2\text{X} + \text{HX}$$

$$\phi\text{—CH}_3 + \text{SO}_2\text{Cl}_2 \xrightarrow{\text{peroxide}} \phi\text{—CH}_2\text{Cl} + \text{SO}_2 + \text{HCl}$$

Consequently, halogenation may be directed specifically to the ring or to the side chain, depending upon the type catalyst used. Iron, aluminum, and their polyhalide salts, FeX_3, AlX_3, induce ring halogenation, whereas illumination and heat lead to side-chain halogenation. The carbon atoms in the side chain are referred to by letters of the Greek alphabet, starting with the one attached to the ring. The *alpha* carbon is activated by the ring and is preferentially halogenated or oxidized.



$$\phi\text{—CH}_2\text{—R} + \text{X}_2 \xrightarrow[\Delta]{h\nu} \phi\text{—}\underset{\substack{|\\ \text{X}}}{\text{CH}}\text{—R} + \text{HX}$$



$$\phi\text{—CH}_2\text{—R} \xrightarrow{\text{oxid.}} \phi\text{—}\underset{\substack{|\\ \text{OH}}}{\text{CH}}\text{—R} \xrightarrow{\text{oxid.}} \phi\text{—}\underset{\substack{\|\\ \text{O}}}{\text{C}}\text{—R} \xrightarrow{\text{oxid.}} \phi\text{—COOH}$$

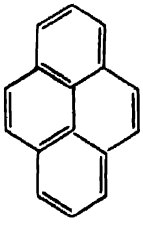
Seldom can the oxidation be stopped at the alcohol or ketone stage, although the ketone can be prepared indirectly from the hydrocarbon by oxidation with CrO_3 (cf. Section 12.2c). Permanganate and dichromate carry the oxidation to the acid. Since it is always the *alpha* carbon that suffers oxidation, all carbon-attached groups may be oxidized to the COOH group.

TABLE 8.1. PHYSICAL CONSTANTS OF SOME ARENES

Name	Formula	Melting Point	Boiling Point	Sp. Gr. (liq.)
Benzene	C_6H_6	5.5	80	0.879
Toluene	$CH_3C_6H_5$	−95	111	.866
o-Xylene	1,2-$(CH_3)_2C_6H_4$	−25	144	.880
m-Xylene	1,3-$(CH_3)_2C_6H_4$	−48	139	.864
p-Xylene	1,4-$(CH_3)_2C_6H_4$	13	138	.861
Mesitylene	1,3,5-$(CH_3)_3C_6H_3$	−45	165	.864
Durene	1,2,4,5-$(CH_3)_4C_6H_2$	80	195	
Hexamethylbenzene	$C_6(CH_3)_6$	165	264	
Ethylbenzene	$C_2H_5C_6H_5$	−95	136	.867
n-Propylbenzene	$CH_3CH_2CH_2C_6H_5$	−99	159	.862
n-Butylbenzene	$CH_3(CH_2)_3C_6H_5$	−81	183	.860
t-Butylbenzene	$(CH_3)_3C_6H_5$	−58	169	.867
Biphenyl	$C_6H_5C_6H_5$	70	255	
p-Terphenyl	$C_6H_5—C_6H_4—C_6H_5$	171		
p-Quaterphenyl	$C_6H_5C_6H_4C_6H_4C_6H_5$	320		
Diphenylmethane	$C_6H_5CH_2C_6H_5$	26	263	
Triphenylmethane	$(C_6H_5)_3CH$	93	360	
Tetraphenylmethane	$(C_6H_5)_4C$	285	431	
Styrene	$C_6H_5CH{=}CH_2$	−31	145	.907
trans-Stilbene	$C_6H_5CH{=}CHC_6H_5$	124	307	
Phenylacetylene	$C_6H_5C{\equiv}CH$	−45	142	.930
Diphenylacetylene	$C_6H_5C{\equiv}CC_6H_5$	63	300	

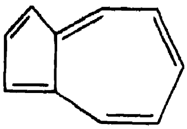
8.3 POLYNUCLEAR AROMATIC HYDROCARBONS

Aromatic hydrocarbons may contain more than one benzene ring. Several phenyl groups may be joined to aliphatic carbon atoms as in triphenylmethane, $(C_6H_5)_3CH$, and 1,2-diphenylethane, $\phi—CH_2CH_2—\phi$; the phenyl groups may be joined together as in biphenyl, $C_6H_5—C_6H_5$; or several rings may be fused together as in pyrene.



Pyrene

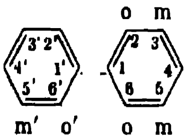
Also, rings other than six-membered rings exist. For instance, azulene contains a seven- and a five-membered ring.



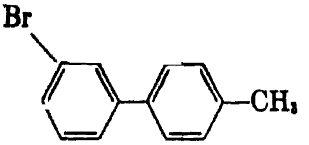
Azulene

Some of these aromatic systems will be discussed.

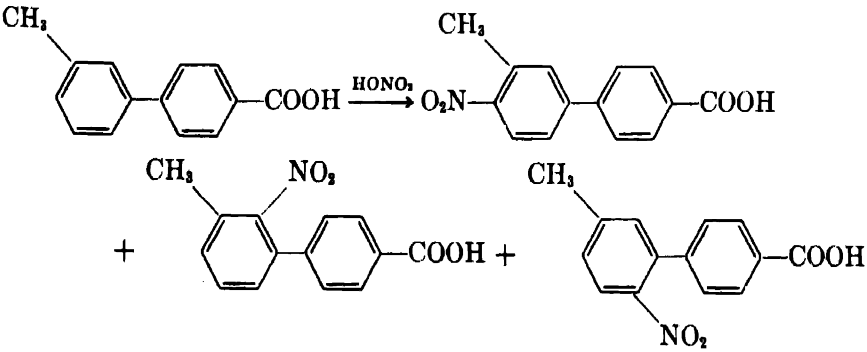
a. Biphenyl derivatives. The simplest two-ring aromatic compound is biphenyl.



The positions in the biphenyl system are numbered or referred to as shown, although either ring may be the primed ring. For illustration,

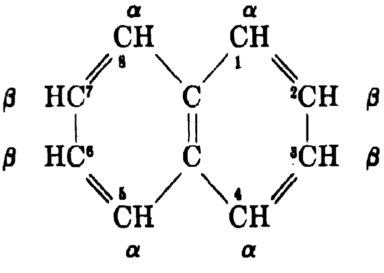


may be called 4-methyl-3′-bromobiphenyl or *p*-methyl-*m*′-bromobiphenyl. Since the Kekulé resonance of each ring is independent of the other ring, either of the two possible Kekulé forms may be written for each ring. The orientation rules for biphenyl are extensions of those for benzene, but a greater mixture of products is obtained than with benzene derivatives. *Nevertheless*, the major products are in accordance with the *o,p*-directing, or *m*-directing effect plus the ring-activating or ring-deactivating effect of substituents. For illustration, in 4-carboxy-3′-methylbiphenyl, the COOH group is ring-deactivating and the CH_3 group is ring-activating; hence, *substitution occurs in the methylated ring, ortho* and *para* to the CH_3 group.



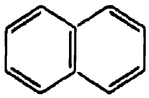
Biphenyl and its derivatives are of some importance. There are four major methods of preparing them, three of which are used primarily for sym-steric hindrance may affect physical properties of molecules. In this case, it has led to optical isomerism.

b. Condensed-ring polynuclear compounds. Naphthalene has two benzene rings sharing a carbon-carbon bond.



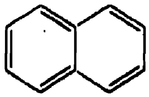
Naphthalene

The positions are numbered or indicated as shown. Thus, in naphthalene there are four *alpha* carbons and four *beta* carbons. Note that the two carbon atoms common to both rings have no hydrogen atoms attached and therefore do not undergo substitution reactions. There are three Kekulé forms that can be drawn for naphthalene. One way to work them out is to draw a Kekulé structure for either ring. Valence rules will then limit the bonding in the other ring to only one possible arrangement.



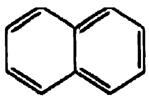
I

Then, draw the other Kekulé form for the first ring (the ring on the left, in this example).



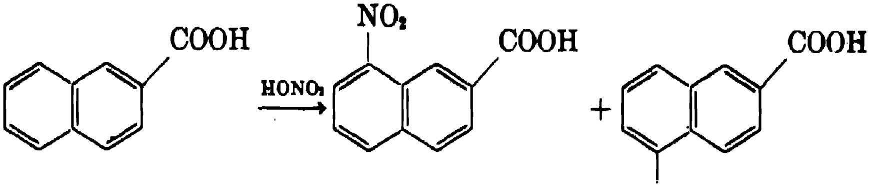
II

Now, looking at the right-hand ring in I, one observes that it has a Kekulé structure; hence, give it the other Kekulé structure. This restricts the bonding in the left ring to one possible structure.

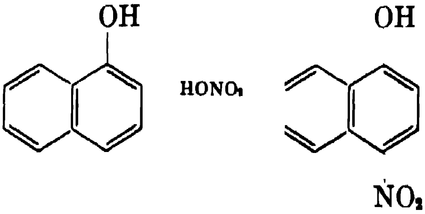


III

The orientation rules for naphthalene derivatives are even less closely followed than those for biphenyl. In general, the *alpha* carbons are the most reactive, and *o,p*-directing groups promote reaction at the attached ring, whereas *m*-orienting groups lead reaction to the other ring.

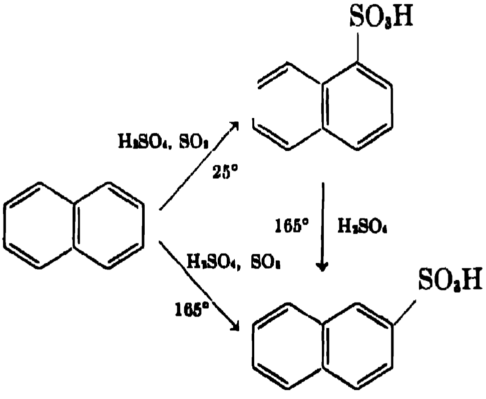


β-Naphthalene-carboxylic acid   8-Nitronaphthalene-2-carboxylic acid   5-Nitronaphthalene-2-carboxylic acid



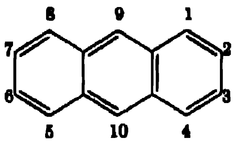
α-Naphthol   1-Hydroxy-4-nitronaphthalene

The position of substitution can be affected by conditions which change kinetically controlled products to thermodynamically controlled products. For example, sulfonation of naphthalene at room temperature produces the faster forming α-isomer.



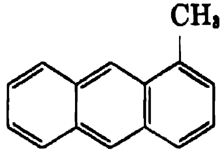
Thus, the transition state for reaction at the α position of naphthalene is more stable than that for reaction at the β position, which leads to a faster formation of the α-isomer. The β-isomer is the more stable, however, owing to steric hindrance from the H atom at the 8 position (*peri* position) to the SO_3H group, and under equilibrium conditions the β-isomer predominates in the product.

Anthracene has three benzene rings fused together side by side. The positions are numbered as shown. There are four Kekulé structures for the

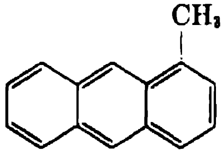


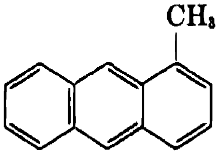
Anthracene

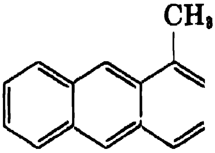
anthracene nucleus. In order to work out the four structures for α-methylanthracene, for example, first give either end ring a Kekulé structure.



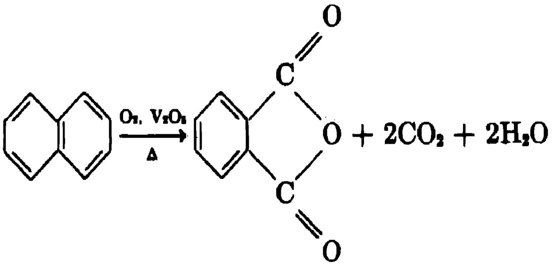
Then, give the same end ring the other Kekulé form. Next, do the same for the other outer ring, thereby getting two more structures, or four in all.







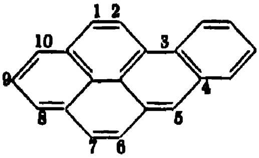
Naphthalene and anthracene are both obtained from coal tar. Naphthalene itself is used as a moth repellent (mothballs). It is also a starting material for the commercial production of phthalic anhydride (used for the production of alkyd plastics, etc.).



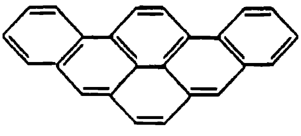
Phthalic anhydride

Various derivatives of naphthalene and anthracene are used as intermediates in the preparation of perfumes, dyes, and other commodities.

Many other polynuclear, condensed-ring aromatic compounds are known. The hydrocarbons have been of extreme interest in recent years because some are very carcinogenic and others are not. Considerable attention has been given to them in an attempt to determine what basic structures lead to carcinogenic properties. Several controversial reports have been made as to whether or not 3,4-benzpyrene, a strong carcinogen, exists in tobacco smoke in sufficient quantity to produce lung cancer. More recently, it has been reported that 3,4,9,10-dibenzpyrene, a more powerful carcinogen than 3,4-benzpyrene, is present in cigarette smoke, but that it can be filtered out and that some filters may already be doing it.



3,4-Benzpyrene



3,4,9,10-Dibenzpyrene

8.4 CLASSIFICATION OF HYDROCARBONS

Several classes of hydrocarbons have been taken up now, and for organization, they may be grouped as follows:

- Aliphatic
  - Saturated alkanes
  - Unsaturated alkenes, alkynes, polyenes
- Carbocyclic
  - Alicyclic
    - Saturated cycloalkanes
    - Unsaturated cycloalkenes
  - Aromatic
    - Alkylbenzenes
    - Biphenyl series
    - Condensed-ring polynuclear naphthalenes anthracenes, etc.

For comparison, some of their chemical properties are given in Table 8.2. The saturated alicyclic and saturated aliphatic hydrocarbons react the same way, and may be grouped together. This is true also for the unsaturated alicyclic and aliphatics. It can be seen from Table 8.2 that the unsaturated aliphatics and alicyclics are easily distinguished from the other two groups

TABLE 8.2. SOME COMPARISONS OF CHEMICAL PROPERTIES OF HYDROCARBONS

	Behavior toward				
Type of Hydrocarbon	Br_2 at 0°	Br_2 at 60° + cat.	Dilute $KMnO_4$	Conc. H_2SO_4, 20°	Conc. HNO_3, 60°–80°
Alkane and cycloalkane	No reaction	Substitution	No reaction	No reaction	No reaction
Unsaturated alicyclic and aliphatic	Rapid addition	Rapid addition	Rapid oxidation	Solution	Explosive oxidation
Aromatic	Negligible reaction	Substitution	No reaction	No reaction	Nitration (yellow product)

but that only nitric acid will permit a distinction between aromatic and saturated hydrocarbons. The general order of their reactivity toward halogens is:

$$\begin{matrix}\text{alkene,}\\ \text{cycloalkene}\end{matrix} > \text{alkyne} > \text{aromatic} > \begin{matrix}\text{alkane,}\\ \text{cycloalkane}\end{matrix}$$

STUDY EXERCISES

1. Give general equations for (a) the Friedel-Crafts reaction, (b) the Wurtz-Fittig, reaction, (c) the Ullmann reaction, (d) the Fittig reaction.
2. Give the structures for (a) 2-methyl-8-bromoanthracene, (b) β-naphthylamine, (c) *o*-methoxy-*m*′-nitrobiphenyl.
3. What is meant by each term (a) dehydrocyclization, (b) resonance energy, (c) Kekulé resonance of naphthalene?
4. What are the industrial sources of toluene, *o*-xylene, naphthalene, biphenyl, benzene, ethylbenzene, and anthracene?
5. Write the four Kekulé structures for anthracene and for biphenyl.

TEST QUESTIONS, Set 8

1. Starting with benzene, how could one prepare in the laboratory (a) $C_6H_5CH_2Br$, (b) *o*-chloroethylbenzene, (c) *p,p*′-dimethylbiphenyl, (d) *p*-isopropylbenzoic acid, (e) *m*-nitrobenzoic acid, (f) *p*-nitrobenzoic acid?
2. What would you expect for the resonance energy of biphenyl relative to that of benzene?
3. How could one distinguish cyclohexane from *o*-xylene by qualitative test-tube experiments?
4. What series of laboratory reactions could one use to prepare toluene from $EtO_2C—(CH_2)_4—CO_2Et$?
5. What experiments could be carried out to distinguish *o*-, *m*-, and *p*-xylenes? They boil within 6° of one another.
6. How could one prepare benzene from toluene?
7. How would the following replacements be made on the benzene ring: (a) H by Cl, (b) Br by C_2H_5, (c) *n*-C_3H_7 by COOH, (d) H by NO_2?
8. Which of the following compounds would exhibit optical isomerism, and explain why or why not in each case: (a) 3,5-dimethyl-3′,5′-dinitrobiphenyl, (b) 2,6-dimethyl-2′-6′-dinitrobiphenyl, (c) 2,2′-dinitro-6,6′-dimethylbiphenyl?
9. Is optical isomerism conceivably possible for 1-(2-bromo-6-ethylphenyl)-1-methyl-2-bromoethylene (α-methyl-β-bromo-2-bromo-6-ethylstyrene)?
10. Why does the $C_1—C_2$ bond of naphthalene have greater double-bond character than the $C_2—C_3$ bond?

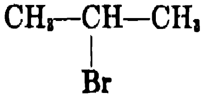
9

Halogen Compounds

Alkyl halides are commonly designated by the formula R—X and aryl halides by ϕ—X, where R and ϕ represent aliphatic and aromatic groups, respectively, and X is a halogen. As stated previously, X does not usually include fluorine since fluorine compounds react and are prepared differently from the rest of the halogen compounds.

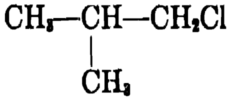
9.1 NOMENCLATURE

When the R group of an alkyl halide, RX, has a trivial name, the alkyl halide is normally named by giving this trivial name and adding the name of the halide. Otherwise, the R group is named according to the Geneva system and the halogen is regarded as a substituent. For illustration, several examples are given, some according to both schemes.



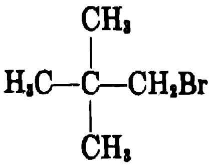
$$CH_3-\underset{\substack{|\\ Br}}{CH}-CH_3$$

Isopropyl bromide
or 2-bromopropane



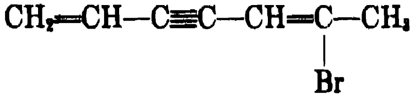
$$CH_3-\underset{\substack{|\\ CH_3}}{CH}-CH_2Cl$$

Isobutyl chloride or
1-chloro-2-methylpropane



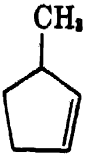
$$H_3C-\overset{\substack{CH_3\\ |}}{\underset{\substack{|\\ CH_3}}{C}}-CH_2Br$$

Neopentyl bromide

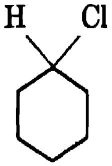


$$CH_2{=}CH-C{\equiv}C-CH{=}\underset{\substack{|\\ Br}}{C}-CH_3$$

6-Bromo-1,5-heptadiene-3-yne

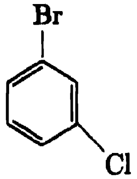


3-Methylcyclopentene

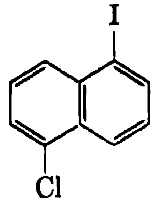


Cyclohexyl chloride
or chlorocyclohexane

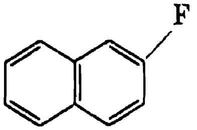
Aryl halides are named as derivatives of the parent hydrocarbon.



m-Bromochlorobenzene



1-Iodo-5-chloronaphthalene



β-Fluoronaphthalene

9.2 PREPARATION

a. Alkyl halides. Alicyclic halogen compounds are included here.

Halogenation: The most obvious way to prepare an alkyl bromide or chloride would be to halogenate the respective alkane. However, as was stressed in Sections 1.2 and 2.7, halogenation of alkanes gives many polyhalogenated products whose separation is difficult in the elementary laboratory. Several more convenient methods of preparing simple alkyl halides are available.

Replacement of OH *by* X: This is a very common method of preparing alkyl halides, because many alcohols are available for starting materials and there are several reagents which may be used to effect the reaction, namely, PX_3, PX_5, HX, and SOX_2. The reactions are a little more complex than is indicated by the following general equations, but the equations can be used for calculating percentage yields:

$$PX_3 \qquad 3ROH + PX_3 \rightarrow P(OH)_3 + 3RX$$

$$PX_5 \qquad ROH + PX_5 \rightarrow RX + POX_3 + HX$$

$$SOX_2 \qquad ROH + SOX_2 \rightarrow RX + SO_2 + HX$$

$$HX \qquad ROH + HX \underset{OH^-}{\overset{ZnCl_2}{\rightleftharpoons}} RX + HOH \qquad HI > HBr > HCl$$

The last reaction is readily reversible, and agents are used to shift the equilibrium in the direction desired. In this case a dehydrating agent is used to drive the reaction toward the alkyl halide. Sulfuric acid is frequently used, but $ZnCl_2$ is better. Tertiary alcohols are dehydrated so easily that sulfuric acid yields more of the respective alkene than alkyl halide. Also, if HI is the halogen acid used, sulfuric acid cannot be employed since it oxidizes the HI to iodine and water.

Addition of halogen acids to alkenes: This is a simple addition of HX to $R_2C{=}CR_2$, discussed in Section 3.4. The rate of addition of the halogen acids decreases in the order HI > HBr > HCl.

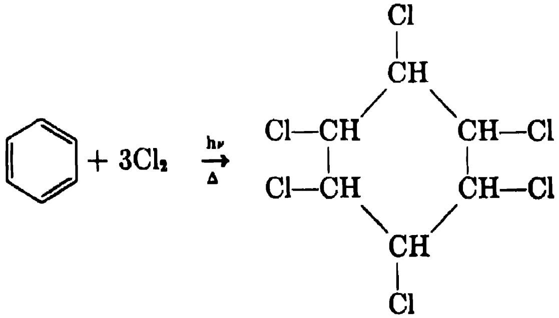
Industrial preparation. The cheapest method of producing alkyl halides, and the one most widely used commercially, is the halogenation of alkanes. The large industrial fractionating columns permit efficient separation of the reaction products, and a stockpile of halogen chemicals is built up to be sold as ordered. Otherwise, complex halogenated compounds are prepared by large-scale adaptations of the laboratory methods.

b. Halobenzenes. Benzene derivatives undergo nuclear halogenation in the presence of Fe, $FeCl_3$, Al, or $AlCl_3$.

$$\phi\text{—H} + X_2 \xrightarrow{\text{Fe}} \phi\text{—X} + HX$$

Only a trace of catalyst is required, and the catalysts are referred to as *halogen carrier catalysts*. The mechanism of this reaction was discussed on page 202. With *m*-orienting groups present, elevated temperatures must be used, but it is possible to substitute all available hydrogen atoms on the ring. Again, halogenation refers only to chlorination and bromination. Fluorination is normally too violent to be carried out directly, and iodination is inconvenient.[1]

It has been stressed that aromatic compounds undergo substitution reactions rather than addition reactions. Nevertheless, in sunlight or strong artificial illumination, benzene will add three moles of chlorine or bromine.



No dichloro or tetrachloro products are recovered; only the hexachloro

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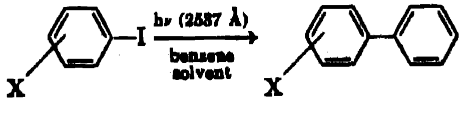
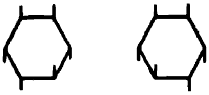
[1] Iodination will take place but the HI formed in the reaction reduces the aryl iodide to reverse the reaction. Therefore, the yields of aryl iodide are poor unless some means is provided of removing the HI as it is formed. This may be done by adding nitric acid to oxidize the HI, but this technique is limited to those aromatic compounds resistant to oxidation by nitric acid. Iodination has also been carried out in the presence of Ag_2SO_4, which precipitates the iodide ion. Sometimes iodine monochloride has been used for iodination.

$$\phi\text{—H} + ICl \rightarrow \phi\text{—I} + HCl$$

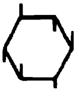
The most common method of preparing aryl iodides is by replacement of the diazonium group as shown on page 408. Aryl iodides have been found to be useful for the synthesis of biphenyl derivatives by irradiating the aryl halide in an organic solvent; e.g.,



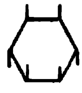
derivative is obtained. The product is 1,2,3,4,5,6-hexachlorocyclohexane; however, it is commonly called *benzene hexachloride*. The carbon ring has the typical *chair* conformation of cyclohexane compounds, and the chlorine atoms assume axial or equatorial positions. This gives rise to eight possible geometric isomers, one of which is asymmetric and may be resolved into two optical isomers. Using a conventional planar representation of cyclohexane rings, we may designate them as follows:



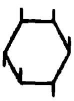
Alpha



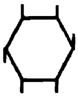
Beta



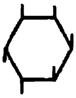
Gamma



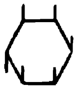
Delta



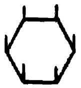
Epsilon



Eta



Theta



Iota

All but the *iota* isomer and the *dextro* form of the *alpha* isomer have been isolated. The benzene hexachlorides are stable compounds, unaffected by hot water, light, and the atmosphere for long periods. They can be recrystallized from hot concentrated nitric acid. In the presence of alkali, even at ordinary temperatures, three moles of HCl are lost, giving a mixture of isomeric trichlorobenzenes.

The *gamma* isomer, called Lindane, is a strong insecticide. Commercial products are mixtures of the geometric isomers and are known under several trade names, some of which are "666," Gammexane, and Gammane. The insecticidal value of a sample of commercial benzene hexachloride depends upon its *gamma* isomer content.

c. **Arylhalomethanes.** As pointed out in Section 8.2, alkylbenzenes can undergo nuclear or side-chain halogenation.

$\phi\text{—CH}_3 \xrightarrow{X_2,\ h\nu} \phi\text{—CH}_2\text{X}$ a benzyl halide

$\phi\text{CH}_3 \xrightarrow{2X_2,\ h\nu} \phi\text{CHX}_2$ a benzal halide

$\phi\text{CH}_3 \xrightarrow{3X_2,\ h\nu} \phi\text{CX}_3$ a benzotrihalide

The benzal chlorides and benzotrichlorides will be of interest when the aldehydes and acids are taken up. The benzyl chlorides may also be prepared by an introduction of the CH_2Cl group into the ring, called *chloromethylation.*

$$\phi\text{—H} + \text{H}_2\text{C{=}O} + \text{HCl} \xrightarrow{\text{ZnCl}_2} \phi\text{—CH}_2\text{Cl} + \text{H}_2\text{O}$$

Chloromethylation takes place by an aldol-type addition of the aryl compound to formaldehyde, and subsequent replacement of the OH by Cl. Two

CH_2Cl groups may enter the ring when *o,p*-directing groups are attached; but, with *m*-orienting groups present, small yields of even the monochloromethylation products are obtained.

Among the arylhalomethanes, the triarylhalomethanes are of special interest because of their use in preparing hexaarylethanes (see page 235). The triarylhalomethanes are usually prepared by one of two methods:

1. Replacement of OH *by* X:

$$\phi_3C\text{—}OH + HX \rightleftharpoons \phi_3C\text{—}X + H_2O$$

This reaction goes very readily in either direction. Good yields of triarylchloromethanes result by merely shaking triphenylcarbinols in concentrated hydrochloric acid.

2. Friedel-Crafts reaction:

$$3\phi\text{—}H + CCl_4 \xrightarrow{AlCl_3} \phi_3C\text{—}Cl + 3HCl$$

Even with excess benzene, the fourth Cl of CCl_4 cannot be replaced by this reaction. Owing to steric hindrance, the intermediate in the Friedel-Crafts reaction between $\phi_3C\text{—}Cl$ and $AlCl_3$ cannot be formed, and, therefore, no tetraphenylmethane is formed.

9.3 PHYSICAL PROPERTIES

The alkyl halides are very sparingly soluble in water, soluble in most organic liquids, and have sweetish odors. For a given halide (cf. Table 9.1), the melting points, boiling points, and densities increase with increasing size of the alkyl group. The alkyl chlorides are less dense than water, and the alkyl bromides and iodides are more dense. This is true only for monohalogenated alkyl halides.

Halobenzenes have physical properties similar to those of benzene. They are insoluble in water, concentrated acid, and base, volatile in steam, and inert to permanganate.

9.4 CHEMICAL PROPERTIES

Because of the large variety of chemical reactions which the alkyl halides will undergo and the commercial availability of all common alkyl halides, they are extremely important in organic synthesis and hold a strategic position in the organic chemical industry. In Section 9.4e it will be noted that a large number of classes of compounds can be prepared from alkyl halides. The alicyclic halogen compounds behave essentially like the alkyl halides. Halobenzenes undergo most of the reactions to be discussed for the alkyl halides, but the halobenzenes are much less reactive and sometimes require conditions not conveniently attained in the elementary laboratory.

TABLE 9.1. PHYSICAL CONSTANTS OF SOME HALOGEN COMPOUNDS

ALKYL HALIDES

Name	Chloride		Bromide		Iodide	
	Boiling Point	Sp. Gr. (liq.)	Boiling Point	Sp. Gr. (liq.)	Boiling Point	Sp. Gr. (liq.)
Methyl	−24		5		43	2.279
Ethyl	12.5		38	1.440	72	1.933
n-Propyl	47	0.890	71	1.335	102	1.747
n-Butyl	78.5	.884	102	1.276	130	1.617
n-Pentyl	108	.883	130	1.223	157	1.517
n-Hexyl	134	.882	156	1.173	180	1.441
n-Heptyl	160	.880	180		204	1.401
n-Octyl	185	.879	202		226	
Isopropyl	37	.859	60	1.310	89.5	1.705
Cyclohexyl	143		165			
Vinyl	−14		16	1.517	56	
Allyl	45	.938	71	1.398	103	1.848
Benzyl	179	1.102	201		93/10mm	
Dihalomethane	40	1.336	99	2.49	180*d*	3.325
Haloform	77	1.595	190	3.42	subl.	4.32

ARYL HALIDES

Name	Melting Point	Boiling Point	Melting Point	Boiling Point	Melting Point	Boiling Point
Fluorobenzene	−45	85				
Chlorobenzene	−45	132				
Bromobenzene	−31	156				
Iodobenzene	−31	189				
Hexachlorobenzene	228	332				
	Ortho		*Meta*		*Para*	
Fluorotoluene		115	−111	115		116
Chlorotoluene	−34	159	−48	162	8	162
Bromotoluene	−26	182	−40	184	28	185
Difluorobenzene	−34	92	−59	83	−13	89
Dichlorobenzene	−17	180	−24	173	52	175
Dibromobenzene	6	221	−7	217	87	219
Nitrochlorobenzene	32	245	48	236	83	239
Bromoanisole		222			11	223
Bromochlorobenzene		199			67	196
Bromoiodobenzene		257			92	252

a. Reduction. The reduction of alkyl halides to alkanes was discussed in Section 2.3a as a method of preparing alkanes.

$$RX \xrightarrow{\text{red.}} RH$$

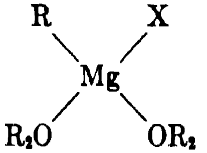
Five reducing agents were presented, namely, H_2 + cat., Zn + HCl, HI + P, $LiAlH_4$, and Mg then H_2O.

b. Wurtz reaction. This reaction also was discussed in Section 2.3a as a method of preparing alkanes.

$$2RX + 2Na \rightarrow R{-}R + 2NaX$$

The Wurtz-Fittig, Ullmann, and Fittig reactions of halobenzenes were given in Sections 8.1 and 8.3.

c. Grignard formation. The Grignard formation is fascinating to watch. One takes an ether solution of an alkyl halide and suspends dry magnesium metal in it. Upon gently warming the mixture, the magnesium metal slowly disappears. What happens is that the magnesium reacts with the alkyl halide to form a metallo-organic substance, R—MgX, which dissolves in the ether solvent because of solvation (recall that when ions dissolve in water they become hydrated). In this case, the ether molecules form weak covalent bonds with the magnesium, and effectively dissolve the Grignard reagent.



The reagent was developed but not discovered by Victor Grignard, and such compounds are named after him.[2] They are soluble in ether solvents owing to the solvation described above, but not soluble in all organic solvents. They readily react with any substance having an active hydrogen, and therefore, the ether solvent must be absolutely dry. Moist ether prevents their formation.

Grignard reagents have two very typical chemical properties, which are (1) to react with compounds having active hydrogen atoms, and (2) to add to carbonyl groups (cf. Section 12.2b). In the former type of reaction, the R group of the Grignard reagent always combines with the active hydrogen atom to form R—H. Because of these two types of reactions, Grignard reagents are used in the preparation of alkanes, alkynes, alcohols, and several other classes of compounds.

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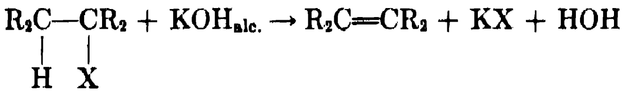
[2] M. S. Kharasch and O. Reinmuth, *Grignard Reactions of Nonmetallic Substances*, Prentice-Hall, Inc., New York, 1954. Victor Grignard, a French organic chemist, received the Nobel Award in chemistry together with P. Sabatier in 1912. The correct formula of the Grignard reagent still is not known with certainty, but R—MgX can be used for making stoichiometric calculations and writing equations.

Grignard reagents may be formed from aryl and vinyl halides too, but with more difficulty than from alkyl halides. Often the use of a higher boiling solvent, such as tetrahydrofuran, leads to successful Grignard formation. Grignards serve as a convenient means of removing a halogen atom from the ring:

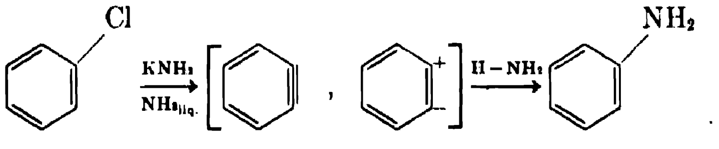
$$\phi\text{—X} \xrightarrow{\text{Mg}} \phi\text{MgX} \xrightarrow{\text{H}_2\text{O}} \phi\text{—H}$$

d. Dehydrohalogenation. The following reaction was discussed in Section 3.2a as a method of preparing alkenes.



$$\underset{\text{H}}{\text{R}_2\underset{|}{\text{C}}}\text{—}\underset{\text{X}}{\underset{|}{\text{CR}_2}} + \text{KOH}_{\text{alc.}} \rightarrow \text{R}_2\text{C}{=}\text{CR}_2 + \text{KX} + \text{HOH}$$

When a halobenzene is treated with a very strong base such as potassium amide, dehydrohalogenation occurs to give an intermediate called a benzyne.



e. Replacement reactions. The alkyl halides react with many types of reagents in an "exchange-partners" manner. Some of these reactions can be tabulated as in Table 9.2.

TABLE 9.2. ALKYL HALIDE REACTIONS

Type reaction: R—X + A—B → R—B + A—X

	Alkyl Halide	Reagent A—B	Product R—B		Side Product A—X
			Formula	Class	
1.	R—X	KOH	ROH	Alcohol	KX
2.	R—X	R′OK	R—O—R′	Ether	KX
3.	R—X	KCN	RCN	Alkyl cyanide	KX
4.	R—X	KSH	RSH	Mercaptan	KX
5.	R—X	KNO_2	RNO_2	Nitroalkane	KX
6.	R—X	AgCN	RNC	Alkyl isocyanide	AgX
7.	R—X	HNH_2	RNH_2	Amine	NH_4X
8.	R—X	NaC≡CR′	RC≡CR′	Alkyne	NaX
9.	R—X	NaR	R—R	Alkane	NaX

Several other less common reagents could be listed. Reactions 1–7 will be discussed later as the respective classes of compounds are taken up; reactions 8 and 9 have already been used.

Thus it can be seen that alkyl halides are important compounds in organic synthesis because they serve as starting materials for the preparation of a large number of classes of compounds. In addition to the nine listed above in the table, alkyl halides are used to prepare alkenes by means of dehydrohalogenation, to prepare alkanes by reduction, to prepare alcohols, aldehydes, or acids via Grignard reagents (to be taken up later), and to prepare several other classes of compounds by a variety of reactions. Also, there is the advantage that essentially all common alkyl halides are commercially available, so that a person can buy them rather than having to prepare them before starting a particular synthesis.

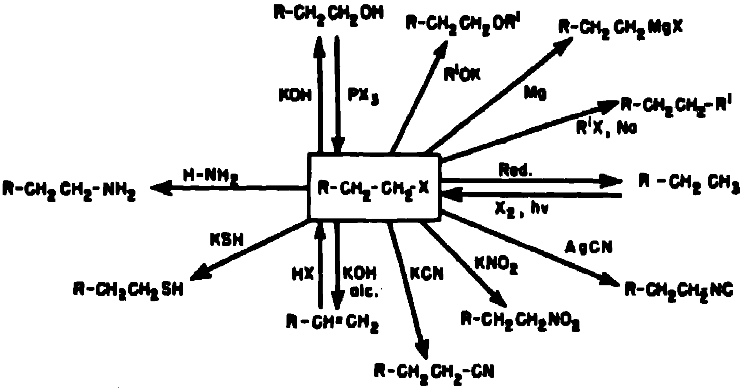


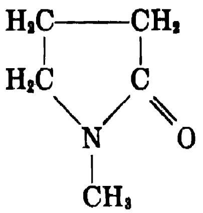
Fig. 9.1. Characteristic reaction chart for alkyl halides.

Aryl halides undergo these same reactions but require more drastic conditions. Thus, alkyl halides hydrolyze smoothly in boiling water but aryl halides require temperatures near 200°. Vinyl halides and aryl halides are alike in this respect. Often the use of a suitable solvent to produce a homogeneous reaction medium is the factor responsible for the success of a particular reaction. For instance, the replacement of X in alkyl halides by NO_2 gave poor yields until an organic solvent was found to dissolve the KNO_2[3a], and it was impractical to replace X by CN[3b] in aryl halides until it was discovered that N-methylpyrrolidone may be used as a solvent for reacting aryl halides with CuCN:[3c]

---

[3] (a) N. Kornblum, *et al.*, *J. Amer. Chem. Soc.*, **78**, 1497 (1956). (b) Dimethyl sulfoxide is a good solvent when one uses alkyl chlorides, which otherwise are slow to react (R. A. Smiley and C. Arnold, *J. Org. Chem.*, **25**, 257 (1960); L. Friedman and H. Shechter, *ibid.*, 877). (c) M. S. Newman and H. Boden, *J. Org. Chem.*, **26**, 2525 (1961).

$$\phi\text{—X} + \text{CuCN} \xrightarrow[\Delta]{\text{N-Methylpyrrolidone}} \phi\text{—CN} + \text{CuX}$$

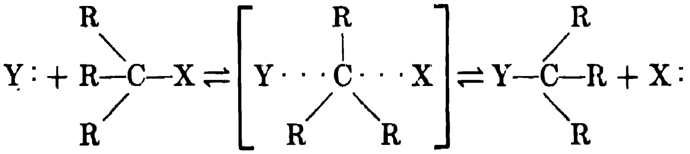


N-Methylpyrrolidone
B.p. 202°
Completely miscible with water
and most organic solvents.

Substituents may also affect the reactivity of aryl halides. Meta-directing groups activate halogens when *ortho* or *para* to the halogen atoms. For example, *p*-nitrochlorobenzene may be hydrolyzed readily near 130°, 2,4-dinitrochlorobenzene below 100°, and 2,4,6-trinitrochlorobenzene is as reactive as an acid chloride. The general effects of structure upon reactivity of halogen compounds are discussed in the next section.

9.5 REACTIVITY VS. STRUCTURE OF HALOGEN COMPOUNDS

a. Replacement reactions. It was shown in the preceding section that alkyl halides undergo a large number of reactions, and most of these take place by either a displacement or an ionic mechanism. In the displacement reaction, a reagent approaches a carbon atom and gradually forms a bond with it while the bond holding the atom or group to be displaced is simultaneously weakened and eventually broken.



The structure in brackets is visualized as the transition state, in which Y and X are both weakly bonded to the carbon atom. Observe that there is an inversion of the tetrahedron in going from R_3C—X to Y—CR_3. The tetrahedron inverts just as an umbrella might turn inside out in a windstorm. Such an inversion is called a *Walden inversion* and usually takes place in a displacement reaction. It is easily detectable with asymmetric carbon atoms, for if the three R groups are different, making the carbon asymmetric, the optical activity of R_3C—X will generally be opposite to that of Y—CR_3. In such a case, the rate of isomerization will equal the rate of reaction. This is the major point in support of the displacement mechanism of reaction.

These displacement reactions are fairly common for nucleophilic reagents, and the reaction tends to go in the direction in which the stronger base displaces the weaker base. The greater the difference in basicity of Y and X, the faster will be the reaction. The order of decreasing basicity of some common anions is:

$$CH_3^- > NH_2^- > OR^- > OH^- > I^- > Br^- > Cl^- > F^-$$

Thus, at comparable concentrations, OH^- tends to replace the halide ions,

$$OH^- + R{-}X \rightarrow R{-}OH + X^-$$

whereas the halide ion does not replace NH_2^- to any measurable degree.

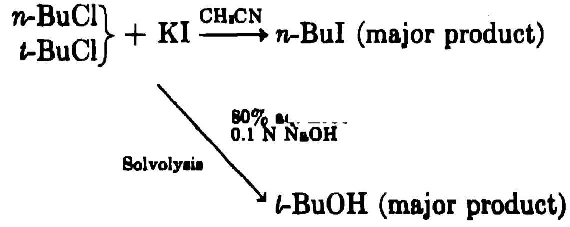
The displacement reaction involves the collision of molecular species (Y and X—Z, or Y—X and Z), and such a reaction is called *bimolecular.* Therefore, this nucleophilic displacement reaction has been abbreviated S_N2. The rate of reaction in the forward direction is proportional to the concentrations of both Y and X—Z. Because the R groups (being much larger than hydrogen atoms) block the backside approach of Y to form the transition state, tertiary alkyl halides favor reaction by a different mechanism.

$$R_3C{-}X \xrightarrow{\text{slow}} R_3C^+ + X^-$$

$$Y^- + R_3C^+ \xrightarrow{\text{fast}} R_3C{-}Y$$

That is, the alkyl halide ionizes to a small extent, and the resulting carbonium ion quickly reacts with the reagent Y^-. The rate of reaction in this case depends solely upon the rate of ionization, which is proportional to the concentration of $R_3C{-}X$. It is, therefore, a unimolecular reaction and is abbreviated S_N1. Thus, primary carbons react by the S_N2 mechanism, tertiary carbons by the S_N1 mechanism, and secondary carbons react by both pathways.

The nature of the solvent can have a pronounced influence on the course of the reaction, and often the solvent is a reactant in the reaction, called *solvolysis.* Thus, an alkyl halide or tosylate ($R{-}SO_3C_6H_4{-}CH_3{-}p$) may react with water to give an alcohol, with a carboxylic acid to give an ester, or with an alcohol solvent to give an ether. In an ionizing solvent, i.e., one that promotes ionization, the ionic S_N1 mechanism is facilitated, whereas a nonionizing solvent favors the S_N2 mechanism. For illustration, *n*-butyl chloride reacts with potassium iodide in acetone or acetonitrile much faster than does *t*-butyl chloride, whereas *t*-butyl chloride is the faster reacting in 80% aq. ethanol (80% EtOH, 20% H_2O) plus 0.1 *N* NaOH.



The base is added in the solvolysis reaction to tie up the HCl as it is formed.

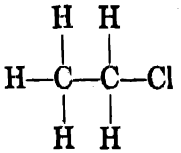
Mechanisms for elimination reactions of alkyl halides were given in Section 3.2 and the stereochemical features were presented in Section 5.4.

For a given organic group, the reactivity of alkyl halides varies with the type of halogen in the order I > Br > Cl. The differences are quantitative rather than qualitative; however, the structure of the organic group may have a much larger effect upon the reactivity of an alkyl halide. For example, allyl halides, $CH_2{=}CH{-}CH_2{-}X$, hydrolyze in water at room temperature, reaction being detectable by precipitation of the halide ion with silver ion.

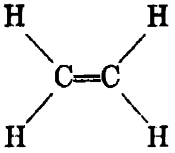
$$CH_2{=}CH{-}CH_2{-}X + H_2O \xrightarrow{25^\circ} CH_2{=}CH{-}CH_2OH + H^+ + X^- \xrightarrow{Ag^+} AgX$$

Of course, the reaction is speeded up by the presence of hydroxide ion. On the other hand, alkyl halides can be shaken with water at room temperature for an hour or so with only a small amount of hydrolysis taking place, if any. If the mixture is heated—for example, to the boiling point of water—the rate of reaction is appreciable. Then again, vinyl halides, $CH_2{=}CH{-}X$, undergo no significant hydrolysis even at 100°; but hydrolysis will take place at a practical rate at 200°. Toward all reagents, this is the relative order of these aliphatic halides: allyl $\gg$ alkyl $\gg$ vinyl. This sequence can be accounted for in terms of the resonance theory. It will be recalled from the discussion in Section 7.2 that a structural formula can be used to represent a molecule as long as the structure is consistent with all properties observed for that molecule. For example, the structural formula CH_3CH_2Cl can be used to interpret all the known properties of ethyl chloride. With excess sodium metal one would expect to get *n*-butane; with sodium ethoxide one would expect to get ethyl ether; with sodium hydroxide one would expect to get ethyl alcohol; and with alcoholic potassium hydroxide one would expect to get ethylene. All these expectations are met, of course. Also, the structural formula of ethyl chloride is consistent with its observed physical properties.

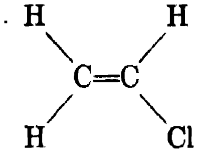
There are many compounds whose structures cannot be represented by a single structural formula. That is, chemists are unable to draw one structural formula (or construct an atomic model) which is consistent with all the properties of that given compound. One structure may explain some of the properties, whereas a different structure must be used to account for other properties. For example, why should the chlorine be so much harder to replace in vinyl chloride, $CH_2{=}CH{-}Cl$, than it is in ethyl chloride? Perhaps the chlorine is held on in a different way in the two compounds. Furthermore, when the bond distances in vinyl chloride are measured, it is found that the C═C bond distance is different from that found in simple alkenes, and the C—Cl bond length of vinyl chloride is different from the C—Cl bond length of simple alkyl chlorides. For example,



C—C = 1.54 Å
C—Cl = 1.76 Å

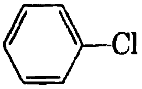


C=C = 1.33 Å



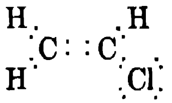
C=C = 1.34 Å

C—Cl = 1.72 Å



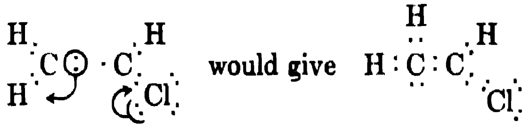
C—Cl = 1.69 Å

Thus, in vinyl chloride, the C=C bond is longer than normal, and the C—Cl bond is shorter than normal. The valence-bond dashes used in structural formulas represent shared electron pairs, it will be remembered, and the electronic structure for vinyl chloride might be that in structure I:

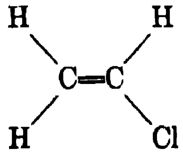


I

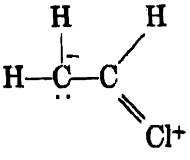
Suppose that one electron pair on chlorine moves in between carbon and chlorine, and that one of the double-bond electron pairs migrates out on the β-carbon atom. That is,



If formal charges (see Section 1.1) are determined, the β-carbon has a negative charge and the chlorine atom a positive charge, as in II:



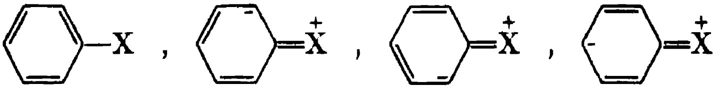
I



II

But notice that the carbon-carbon bond in II is a single bond and that the carbon-chlorine bond is a double bond. Since single bonds are longer than double bonds, the carbon-carbon distance in II is greater than in I, and the carbon-chlorine distance in II is shorter than in I. Since the experimentally observed values are between the normal C—C and C═C bond values, chemists say that the actual structure of vinyl chloride is neither I nor II, but some intermediate structure which cannot be indicated by any single structural formula. In other words, vinyl chloride has a certain resemblance to I and a certain resemblance to II. It will undergo addition reactions to the carbon atoms, a fact which provides evidence for I. At the same time the chlorine is hard to replace, a fact which suggests a strong bond, such as a double bond, between the carbon and chlorine atoms. Also, physical properties, such as the bond distances and dipole moments reveal the resemblance of vinyl chloride to structure II. Therefore, the actual structure of vinyl chloride is neither I nor II, but a composite of I and II, i.e., something in between the two. This is what is called *resonance*. It is a circumstance in which more than one structural formula must be given to represent all the observed properties of a compound, the compound actually having no one of the proposed structures but a weighted composite of them all.

Similarly, the inertness of aryl halides toward nucleophilic reagents is accounted for in terms of the halobenzene resonance:

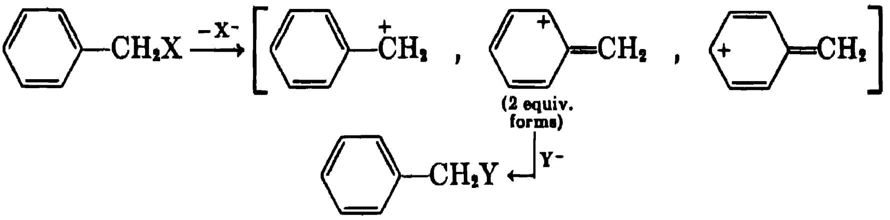


In addition to this phenyl-halogen resonance, there is still the Kekulé resonance of the ring. It can be seen, therefore, that structural formulas for aryl halides are only approximations for the actual structures.

It will be found that whenever resonance does occur for a compound, the compound will be more stable than would be expected on the basis of any single proposed structural formula for that compound. This explains the high reactivity of allyl halides. In the displacement reactions

$$B^- + CH_2{=}CH{-}CH_2X \rightarrow CH_2{=}CH{-}CH_2B + X^-$$

where B^- is some base, if the allyl halide is able to ionize, then the reaction would take place more readily. Now, if the allyl halide were to ionize, it would yield $CH_2{=}CH{-}CH_2^+$. Normally such ions, carbonium ions, are very unstable, but in this case, resonance occurs to stabilize the ion. This does not mean that allyl chloride is ionic, but that it has a tendency to produce the intermediate ion. This facilitates reaction to the extent that hydrolysis occurs even at room temperature. There is no reason to choose between $CH_2{=}CH{-}CH_2^+$ and $^+CH_2{-}CH{=}CH_2$ as the best structure of this carbonium ion.[4] In other words, two equally possible structures can be drawn, and therefore, resonance occurs. When resonance occurs, the molecular species is more stable than expected, and in this case, resonance stabilization of the carbonium ion facilitates reaction of the allyl halide. Accordingly, allyl halides react much more readily than alkyl halides. Likewise, benzyl halides undergo nucleophilic replacements readily because of the relatively stable intermediate carbonium ion.



b. Free radical formation. Because hexaarylethanes are normally prepared from the respective triarylhalomethanes, an unusual property of the hexaarylethanes can be discussed at this time. In 1900, Moses Gomberg was studying the properties of tetraphenylmethane and wanted to prepare hexaphenylethane for purposes of comparison. After several exploratory experiments, he treated triphenylchloromethane (trityl chloride) with finely divided silver metal in the absence of air.

$$2\phi_3C{-}Cl + 2Ag \rightarrow \phi_3C{-}C\phi_3 + 2AgCl$$

He obtained a white crystalline solid which was soluble in benzene to give a deep-yellow solution. The solution was found to react rapidly with oxygen to form a peroxide and to react with iodine in the absence of oxygen to form triphenyliodomethane. Then, he determined the molecular weight of his hexaphenylethane cryoscopically and obtained a value of 383. The molecular weight of hexaphenylethane is 486, and that of triphenylmethyl, $\phi_3C\cdot$, is 243. Gomberg explained these observations by proposing that hexaphenylethane dissociates in solution in the absence of air to give two free radicals.[5]

---

[4] These two structures are regarded as being equivalent and distinct, although they are also identical. However, if one end were labeled with isotopic carbon, then the two would be distinguishable:

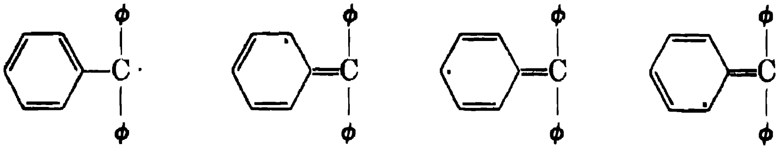
$$C^{14}H_2{=}CH{-}\overset{+}{C}H_2 \quad \text{from} \quad {}^{+}C^{14}H_2{-}CH{=}CH_2$$

[5] In hydrocarbon solvents, hexaphenylethane dissociates to produce neutral free radicals. On the other hand, solutions of hexaphenylethane in liquid sulfur dioxide have a high electrical conductivity. Most textbooks attribute this conductivity to the presence of carbonium and carbanions.

$$\phi_3C{-}C\phi_3 \rightleftarrows \underset{\substack{\text{Triphenyl-}\\ \text{methonium ion}}}{\phi_3C^+} + \underset{\substack{\text{Triphenyl-}\\ \text{methide ion}}}{\phi_3C^-}$$

$$\phi_3C:C\phi_3 \rightleftharpoons 2\phi_3C\cdot$$

Gomberg's experiments attracted the attention of many chemists, and considerable work has been done in this area since then. This is another illustration of the unusual stability of compounds exhibiting resonance. Aliphatic free radicals are too unstable to exist for more than a small fraction of a second (Section 2.4). However, triarylmethyl free radicals are stable in solution, and some are even stable in the solid state. The free radicals are resonance hybrids of many structures in which the odd electron is located on any of the *ortho* or *para* carbon atoms of the three benzene rings.



When substituents that will also accommodate the odd electron are in the ring, the free radicals are further stabilized. The degrees of dissociation of some hexaarylethanes into free radicals are given in Table 9.3.

TABLE 9.3. DISSOCIATION CONSTANTS FOR SOME HEXAARYLETHANES

Substituted Ethane	*K (in benzene near 25°)*
Hexaphenyl	0.0002
Hexa-*p*-tolyl	12
Hexa-β-naphthyl	30
Hexa-*p*-anisyl	120
Hexa-*p*-nitrophenyl	Largely dissociated in solid state

Resonance alone is not responsible for the dissociation of hexaarylethanes. Steric hindrance in the undissociated compound is known to weaken the ethane C—C bond to facilitate dissociation.[6]

There are three general methods used to study the degree of dissociation of hexaarylethanes.

1. Colorimetric: The undissociated ethanes have little or no color, but the free radicals are colored. Hence, the depth of color formed is proportional to the degree of dissociation. This method is far from being quantitative. With the use of a spectrophotometer, it can be made quantitative.

2. Cryoscopic and ebullioscopic: The freezing-point lowering and boiling-point elevation of solvents are due to the number of particles in solution and

It has been shown, however, that the conductivity depends upon the presence of oxygen, and the absorption spectrum of triphenylmethide ion is missing from the spectrum of the solution. The equilibrium is therefore more complex than simple ionization into the carbonium ion and carbanion as commonly expressed.

[6] L. N. Ferguson, *The Modern Structural Theory of Organic Chemistry*, Prentice-Hall, Inc., Englewood Cliffs, N.J., 1963, pp. 355 ff.

provide an old, established method of determining molecular weights. This method has the disadvantage of being applicable only at the temperatures near the freezing or boiling points of the solvents used. Since the degrees of dissociation of hexaarylethanes vary with temperature, it is desirable to make measurements at various temperatures.

3. Magnetic susceptibility: This method is the most widely applicable. It is based on the fact that substances with unpaired electrons are magnetic. In addition to the properties of mass (energy) and electric charge, an electron has the property of spin. Since a rotating charge produces a magnetic field, a spinning electron produces a magnetic dipole whose direction depends upon the direction of spin of the electron. Any atom with an odd number of electrons, and therefore having at least one unpaired electron, will be magnetic. In fact, when we speak of paired electrons, we mean their magnetic dipoles are oriented in opposite directions to cancel each other. All electrons in the hexaarylethane molecule are paired, but the free radicals each have an unpaired electron and are magnetic (the term used is *paramagnetic*). By measuring the magnitude of the magnetic property (the term used for this is *magnetic susceptibility*) of hexaarylethane solutions, the degree of dissociation can be determined.

Trityl halides react with primary alcohols in preference to secondary alcohols. Advantage is taken of this fact to alkylate selectively alcohol groups of carbohydrates (Section 23.2b).

9.6 FLUORINE COMPOUNDS

Monofluoro aliphatics are not greatly different from the other monohalo aliphatics, but since most of the important reactions of the alkyl halides involve removal of the halogen, the alkyl fluorides have little use in this capacity because of the difficulty in breaking the C—F bond. On the other hand, polyfluoro aliphatics are greatly different from the other polyhalo compounds, and the polyfluoro chemicals opened up a new area of organic chemistry. More will be said about them after the simple alkyl fluorides are discussed.

a. Preparation of alkyl fluorides. The most general method of preparing alkyl fluorides is through the replacement of a halogen atom by a fluorine atom:

$$\text{R—X} + \text{MF} \rightarrow \text{R—F} + \text{MX} \qquad \text{MF} = \text{SbF}_3 \text{ (Swarts reaction)}$$
$$\text{HgF}_2\text{, HF, etc.}$$

The alkyl halide is refluxed over the metal fluoride for a given period and then distilled. Usually the reaction is carried out in copper or stainless-steel apparatus. Liquid hydrogen fluoride will serve as well as the metal fluorides.

Anhydrous potassium fluoride in a solvent such as N-methylpyrrolidone has been found to give good yields.

Alkyl fluorides have been produced also by (1) adding hydrogen fluoride to alkenes, (2) replacing the OH group of alcohols by fluorine atoms, or (3) by direct fluorination; but these methods are frequently unreliable. In (1) the reaction must be conducted at low temperatures, −40° to −60°, to minimize polymerization of the alkene and isomerization of the products. Reaction (2) is reversible, with the equilibrium usually on the undesired side, and several side products are produced. With respect to (3), most organic compounds burn or explode when brought into direct contact with fluorine. *Addition* of fluorine to a double bond liberates about 107 kcal/mole, whereas chlorine liberates only 33 kcal. *Substitution* of fluorine for hydrogen liberates 104 kcal, whereas 24 kcal are liberated from chlorine substitution. Thus fluorination liberates enough heat to break most single covalent bonds in organic compounds and liberates at least sufficient heat to ignite many compounds. There are several techniques employed to moderate the reaction. One technique is to dilute the fluorine stream with an inert gas; a second is to use an inert solvent for diluting the reactant, for which CF_4 is frequently chosen. The third technique is to use a container immersed in a low-temperature bath whose inside is crisscrossed with metal sheets to help conduct the heat of reaction to the cold sides. In spite of these several precautions, the most generally successful method of preparing alkyl fluorides in the laboratory is by the Swarts reaction.

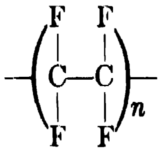
Most aliphatic fluorine substances of importance are polyfluoro compounds, but one commercial monofluoro compound is sodium fluoroacetate, $CH_2F—CO_2Na$. A trade name for it is 1080; it is a very toxic rat poison, but unfortunately, it is also poisonous to human beings.

b. Fluorochemicals. Fluorocarbons, sometimes called *perfluoro chemicals*, are fluorine analogs of hydrocarbons; the latter contain hydrogen and carbon only, and fluorocarbons contain fluorine and carbon only. When more than one fluorine is attached to a single carbon, and particularly when all valences of an aliphatic carbon have fluorine attached, remarkable new properties result. This has led to the development of compounds of unusual value. Even the typical properties of functional groups in fluorocarbon derivatives are sometimes altered.

Preparation of fluorochemicals: In the laboratory, fluorocarbons and their derivatives are generally prepared by the Swarts reaction. Commercially the following three methods are used most extensively: (1) Swarts reaction, (2) addition of HF to olefins, and (3) electrofluorination. This third method is the newest and most practical at present. An organic compound is dissolved in liquid HF and the solution electrolyzed. The process has the advantages of (a) fluorination going to completeness, and (b) the final products, but not the intermediates, being insoluble and separating automatically.

Properties of fluorochemicals: The fluorochemicals have several important, and sometimes unique properties.

1. Unusual stability. Most fluorochemicals resist decomposition at temperatures up to "dull red heat," and are inert to all chemicals, including oxygen and fluorine, up to about this same temperature. For example, a temperature of about 550° decomposes propane, whereas a temperature near 1000° is required to disintegrate perfluoropropane, C_3F_8. Hence, oils, plastics, paints, and rubbers composed of fluorocarbons impart for strategic purposes thermal stability, oxidation resistance, and nonflammability. For illustration, when tetrafluoroethylene, $CF_2{=}CF_2$, is polymerized, the product, called *Teflon*,



is inert to all chemicals. It makes good electrical insulators and gaskets which are to be exposed to caustic reagents, such as fluorine in fluorine generators. It makes an ideal lubricant because it stays slippery at temperatures below −40° and above 300°, does not collect sand or dust, can be sprayed like paint on metal or wood surfaces, and then heat-fused into a coating that sticks like enamel. For this reason it is a "miracle lubricant" for the Armed Services, whose weapons are exposed to all temperatures and get very hot during firing operations. In gun-firing tests, freedom from cartridge-jamming and deposits are far beyond expectations. Another simple application of Teflon coatings is made by commercial bakers. They formerly used large quantities of flour to prevent dough from sticking to pans and dough chutes, but on Teflon-coated surfaces, loaves and pies can be turned out without leaving a crumb.

Trifluorobromomethane, CF_3Br, is a nontoxic fire extinguisher, twice as effective as the old *carbon tet*, CCl_4, which produces highly poisonous phosgene when used for extinguishing fires.

2. Low intermolecular forces. The second valuable property of fluorochemicals is their low cohesive forces. In Section 1.2 was discussed the trend in polarity of compounds from one extreme of ionic compounds (salts) to the other extreme of nonpolar compounds (hydrocarbons). Also the simple generalization that "like dissolves like" was made. Normally substances will either dissolve in polar solvents such as water and alcohols or in nonpolar solvents such as carbon tetrachloride and hydrocarbons. That is, substances are generally waterlike or oillike; the waterlike do not dissolve in oils and the

oillike do not dissolve in water. The fluorocarbons form a third class, however, with little tendency to mix, i.e., "be wetted" either by the waterlike or the oillike liquids. Since most materials commonly encountered are either waterlike or oillike, it is difficult to find anything that will stick to a fluorocarbon surface. Accordingly, fluorocarbon surfaces are readily cleaned from practically everything and are water repellent. Fabrics treated with fluorochemicals are virtually stainproof. Hence, fluorochemical materials make good surface coatings and high-temperature lubricants.

Because of their low intermolecular forces, the fluorochemicals have relatively low boiling points and their vapors approach perfect gas behavior. Many binary mixtures of perfluorochemicals are ideal solutions. Because of their low boiling points, combined with their chemical inertness, the fluorochemicals have other important uses. Mention will be made in Section 9.7a that Freon is a nontoxic, noncorrosive, nonflammable, and odorless refrigerant. These properties which make Freon a good refrigerant, also make it an excellent propellant in aerosol dispensers of insect repellents. The repellents are used extensively in the field as well as in the home (cf. Section 9.7g). In addition, their low flammabilities and low dielectric constants make the fluorochemicals the only suitable materials for liquid coolants in coaxial cables which transmit high-frequency and microwave energy.

3. Electronegative groups. The large electronegativity of fluorine imparts a very large electronegativity to fluorocarbon groups. As a result, perfluoroalkyl amines and ethers do not show basic properties and may be classified as inert fluorochemicals. The fluorocarbon carboxylic acids have acid strengths equal to mineral acids, and their high thermal and oxidation stability makes them very useful as surface-acting agents in highly reactive systems such as nitration and sulfonation reactions. Also, as acid catalysts or oxidizing agents (electron seekers), they are used advantageously for several reactions, some of which will be used in this book (pages 347, 370, 428 and 435).

Perfluoroalkyl groups considerably alter the characteristic properties of functional groups. Some of these will be mentioned when the respective classes of compounds are taken up. For example, the nucleophilic substitution of halogens by OH, NH_2, etc., was discussed in this chapter; however, CF_3I does not undergo such reactions. RX compounds readily hydrolyze at 100° to give $ROH + HX$, but CF_3I yields $CF_3H + IOH$, indicating that the polarization of the C—I bond in CF_3I is $\overset{-}{C}:\overset{+}{I}$ rather than the usual $\overset{+}{C}:\overset{-}{I}$.

9.7 USES OF HALOGEN COMPOUNDS

Halogen-containing organic chemicals are used for a wide variety of purposes, not to mention the numerous types of syntheses outlined in this chapter. In addition to the uses of the perfluoro compounds described in Section 9.6, halogen compounds are used extensively for the following purposes:

a. Refrigerants. To be a refrigerant a substance must have a boiling point not far above room temperature, and it must be transformable from a gas to a liquid by pressure alone at this same low temperature. Sulfur dioxide and ammonia were used as refrigerants for some time, but they have the undesirable properties of being toxic and very irritating. The discovery of Freon provided a nontoxic, odorless, and very effective refrigerant, which is now used almost exclusively. Freons are polychlorofluoro alkanes. Freon 112, a commonly used member, is $C_2Cl_4F_2$.

b. Spreaders. Much of the success of DDT (page 243) and other modern insecticides is due to their efficient distribution by aerosol bombs over agricultural areas, leaves of plants, and in hard-to-reach places. These bombs use Freon as the propellant. Octafluorocyclobutane (Freon C-318) was the first fluorocarbon propellant approved by the Food and Drug Administration for food use. It is used in pressurized cans with "whipped creams," etc.

c. Antiseptics. Iodoform, CHI_3, is an old antiseptic which is still used in some surgical dressings.

d. Fumigants. Methyl bromide is used for fumigation of meat-packing plants. It is able to control rodents, cockroaches, ham beetles, and other vermin without contaminating meat or imparting odor, taste, or toxic residue.

e. Anesthetics. Ethyl ether, or often just ether, $(C_2H_5)_2O$, is the anesthetic generally used, primarily because of its ease of administration and the excellent relaxation of the muscles which it causes (see Section 11.5). It does have certain undesirable effects, among which is its aftereffect of nausea. Other ethers and certain halogenated compounds, such as chloroform, $CHCl_3$, vinyl chloride, $CH_2{=}CHCl$, and ethylene chloride, $CH_2Cl{-}CH_2Cl$, each offer certain advantages over ethyl ether, but none has found extensive use yet.

f. Solvents. Alkyl halides are used as solvents for dry cleaning (carbon tetrachloride is an old familiar one), for degreasing metals, and for low-temperature extraction processes.

g. Pesticides. Aromatic and alicyclic halogen compounds find extensive use as pesticides because of their toxic properties. It is therefore an appropriate time to discuss pesticides. The term *pesticide* has come into use in recent years to refer to chemicals used for the protection of man and his possessions, domestic animals, crops, and forests against attack by insects, plant diseases, weeds, rodents, etc. The objective is to have a maximum control of pests with a minimum of damage to other forms of plant and animal life. The focus of attention on the first factor with frequent neglect of the second brought on much public criticism in 1962 on the use of pesticides, triggered by Rachel Carson's *Silent Spring*. However, subsequent governmental programs and controlled use of pesticides have improved their effective application.

All through history, man has waged a constant fight against insects, and although many triumphs have been achieved, insects still threaten man's welfare. It would be impossible to produce an adequate world supply of food today without the use of pesticides. Entomologists estimate that there are about 1,000 household insects per person in the United States alone, and there are many times this number of outdoor pests. If man were to let up in the fight for just 24 hours, he would be completely overcome. An example of what an unchecked plant disease can do is the 1845 invasion of Ireland by potato blight. It destroyed Ireland's chief food crop, killed 12 per cent of the population, and forced another 18 per cent to leave the country. There is no attempt to wipe out the scavengers completely; man hopes merely to reduce them to a nuisance value rather than the menace they now present. Even in the face of effective aerosol bombs and specially designed pesticides of high potency, insect populations continue to grow.

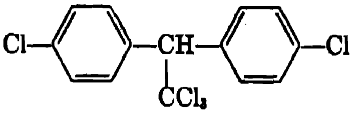
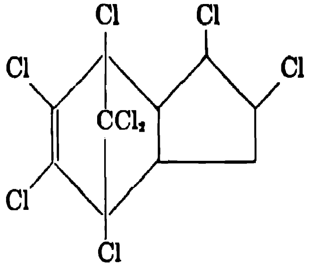
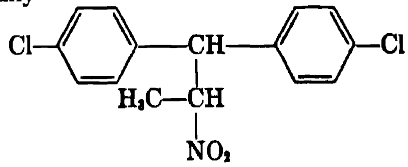
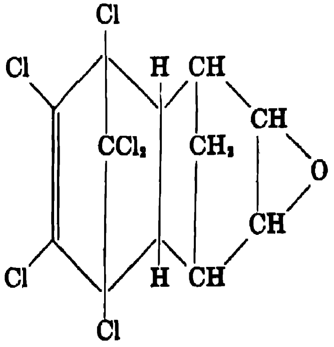
In this country alone, there are 85,000 kinds of insects, mites and other pests. About 6,500 of these are considered destructive, and about 600 major insect pests cause an annual crop and livestock loss of over $4 billion.

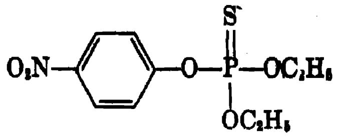
One hundred different insects, including the codling moth, inflict 30 to 40 million dollars' worth of damage each year on apple trees and they could not be grown economically without chemical control. Spraying with DDT and other chemicals has reduced the yearly loss of cotton by the boll weevil from $1 billion to a fourth of that amount. Note that the losses are in billions of dollars, not just millions. In attempting to keep insects under control on farms and indoors in the United States, about $400 million is spent annually.

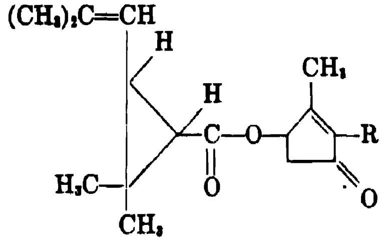
The principal household offenders are the clothes moth, flies, mosquitoes, roaches and carpet beetles. Some of the most destructive farm pests are the grasshopper, the corn earworm, the Mexican bean beetle, cotton aphids, potato beetles, certain fungi, and, of course, grass weeds. Among the insects which plague cattle mercilessly is the horn fly.

To combat these pests, both space and surface sprays are used. A surface spray is intended for crawling insects. It contains a residual toxic compound that will kill weeks after application. The space spray is used against flying insects. The usual propellants for aerosol bombs are fluorocarbon gases such as Freon.

At the close of World War II, DDT ushered in the era of synthetic insecticides. Now, industry has introduced many other potent ones, of which only a few can be mentioned.

General household and field insecticides:	*Remarks*
DDT	 1,1,1-Trichloro-2,2-bis-(*p*-chlorophenyl)-ethane
Lindane	Benzene hexachloride. Particularly good against the boll weevil, the cotton aphid, and the locust
m-Delphene	Diethyl toluamide. Can be applied in alcohol solution directly on the skin. Gives a pleasant lotion feeling. Very good mosquito repellent
2-Ethyl-1,3-hexanediol	
Naphthalene *p*-Dichlorobenzene	Most common solid moth repellents
Chlordan	 Irritating to skin and highly toxic internally
Prolan	
Methoxychlor	Methoxy analogue of DDT. Can be used in dairies and does not impart toxicity or taste to milk
Dieldrin	 Cl Cl H CH CH CCl₂ CH₂ O CH Cl H CH Cl

Parathion	
Pyrethrin	The most potent insecticidal constituent of pyrethrin flowers. Pyrethrin is a variety of Chrysanthemum grown in Western Asia, Africa, and South America. In hydrocarbon solvents, pyrethrin is highly potent against household pests and is completely nontoxic to humans and animals
Allethrin	A synthetic material having insecticidal properties similar to pyrethrin, and also effective against insects resistant to DDT



Pyrethrin, R = $CH_2{-}CH{=}CH{-}CH{=}CH_2$

Allethrin, R = $CH_2{-}CH{=}CH_2$

Thanite and Lethane (thiocyanates) Lead arsenate Calcium arsenate	Very toxic to man
Herbicides:	
2,4-D 2,4,5-T	2,4-Dichloro- and 2,4,5-trichlorophenoxyacetic acids. Unusually good weed and brush eliminators. Nontoxic to livestock. Are plant hormones which stimulate abnormal growth followed by death of deep-root plants
Fungicides:	
Pentachlorophenol	Spread at base of houses for protection against wood ticks, and coated on military equipment for protection against fungi
Copper lactate and naphthenate Phenylmercuric compounds	Among the best. Very active, least toxic to man, odorless, and withstand leaching
Sodium propionate	A mold inhibitor in bakery products
Fumigants:	
HCN	One of the oldest in use
CH_3Br	Used in meat packing plants

Rodenticides:	
1080	Sodium fluoroacetate. Extremely potent, but toxic to all animals and man
ANTU	α-Naphthylthiourea. Strong rodenticide but toxic to man. Attacks the lungs and drives animals out in the open where they die in 10–24 hours after ingestion
Lampreycides:	
2770 (*m*-Trifluoromethyl-4-nitrophenol)	Used in the Great Lakes to kill the lampreys, which otherwise kill the fish.

Just as germs build up a resistance to drugs, insects slowly become resistant to insecticides. For example, after the war, DDT would wipe out flies and mosquitoes almost entirely where it was used. Then a few years later, strains of flies and mosquitoes were found to be unaffected by DDT. Entomologists turned to other chemicals for fly control. For a while, Lindane, Methoxychlor, and others were active against DDT-resistant flies and mosquitoes; then these too lost their effect. In another case, thrips in California citrus groves were controlled for several years by tartar emetic. Over a period of seven to nine years the thrips built up a resistance to tartar emetic, rendering it of little use. DDT was then employed effectively, but in three to six years the thrips also became DDT-resistant. Now, for the past three to four years, Dieldrin has been used satisfactorily.

Since it takes from 20–40 generations to develop a high level of resistance, some insects like the codling moth and the corn borer can be controlled by a single insecticide over a 10–20 year period. When an insect does become resistant to one insecticide, it usually has some resistance to chemically similar insecticides. Hence, the different insecticide used should be one having a markedly different structure. Also, synergists—compounds which activate insecticides but are harmless when used alone—increase the effectiveness of insecticides. Although synergists are usually structurally related to a given insecticide, e.g., $(ClC_6H_4)_2CH—CH_3$ is a synergist for DDT $(ClC_6H_4)_2CH—CCl_3$, this is not always the case, because

$$p\text{-}Cl—C_6H_4SO_2N(C_4H_9\text{-}n)_2$$

is also a powerful synergist for DDT.

Hence the fight against insects continues, but man is using new and more effective weapons. Over 100 different pesticides are in commercial use today. A new technique is to use *chemosterilants*, whereby an agent is used to sterilize one sex of a particular pest so that the species is soon eradicated. Sex attractants are also being used to lure one sex of a specific pest. The sex attractant is mixed with a pesticide so that the pest is wiped out without the pesticide coming in contact with the plants. This avoids any possible residue on foods. Gyplure, the sex attractant of the gypsy moth, is one of the most powerful biologically active chemicals known; as little as 10^{-14} micrograms will attract the gypsy moth.

STUDY EXERCISES

1. Illustrate by general equations four methods of preparing alkyl halides.
2. What reagents and conditions would be used to convert ethyl bromide into

(a) ethyl alcohol
(b) ether, $(C_2H_5)_2O$
(c) ethane
(d) nitroethane
(e) ethyl cyanide
(f) ethylene
(g) ethyl mercaptan, C_2H_5SH
(h) ethylamine, $C_2H_5NH_2$
(i) ethyl isocyanide, C_2H_5NC

3. State several uses of halogen compounds other than for chemical synthesis, and for each use name a specific compound which is employed.

4. What is the order of ease of hydrolysis of the halogen in $(CH_3)_3C—Cl$; $CH_3CH_2CHICH_3$; $CH_2═CH—CH_2Br$; $CH_3CH_2CHBrCH_3$; $CH_3CH_2CH_2I$, and $CH_2═CHCl$?

5. Do alkyl halides ionize when in contact with water? How could this be verified?

6. Why are alkyl bromides often used in the laboratory in preference to the chlorides?

7. How may aliphatic fluorine compounds be prepared in the laboratory?

8. Give general equations for two methods each of preparing benzyl halides and triarylhalomethanes.

9. Give an equation for the chloromethylation of toluene.

10. Give equations for the reaction of benzyl bromide with KCN, KOH, KNO_2, Mg, C_2H_5Na, and C_6H_5Li.

11. What are free radicals? Why is triphenylmethyl more stable than triethylmethyl?

12. Most primary alcohols react with HBr by the S_N2 mechanism, but neopentyl alcohol appears to react by the S_N1 mechanism. Offer an explanation for this difference in mode of reaction.

TEST QUESTIONS, Set 9

1. What series of reactions could be used to prepare isopropyl bromide from *n*-propyl bromide?

2. Mention one or two reasons why the organic halogen compounds used as solvents in industry are chlorides rather than bromides or iodides.

3. How could one prepare 1,1-dibromoethane and 1,2-dibromoethane?

4. What volume of methane, measured at 190 mm of mercury and −136°, would be produced by the hydrolysis of 11.93 g of methylmagnesium bromide?

5. How could one distinguish by qualitative test-tube experiments (a) allyl chloride from *n*-propyl chloride, (b) allyl bromide from vinyl bromide, (c) $CH_2═CH—CH_2CH_2Br$ from $CH_2═CH—CH_2Br$, (d) *n*-pentyl bromide from 5-bromo-1-pentene?

6. What volume of 5 *N* NaOH would be required to neutralize the acid liberated in the hydrolysis of 61.5 g of isopropyl bromide?

7. What effect should the resonance of vinyl chloride have on the dipole moment of the compound?

8. What series of laboratory reactions could be used to prepare the following,

starting with benzene in each case: (a) *m*-bromobenzoic acid, (b) *m*-nitrochlorobenzene, (c) *p*-methylbenzyl alcohol, *p*-CH_3—C_6H_4—CH_2OH?

9. What series of laboratory reactions could be used to convert *o*-bromobenzyl chloride, *o*-Br—C_6H_4—CH_2Cl, to *m*-nitrobenzenesulfonic acid, *m*-O_2N—C_6H_4—SO_3H?

10. How could one distinguish by qualitative test-tube experiments (a) *p*-chlorotoluene from 1-chloro-4-methylcyclohexane, (b) chlorobenzene from toluene, (c) benzene hexachloride from hexachlorobenzene?

11. Does the *alpha* isomer of benzene hexachloride have a plane of symmetry? Can it be superimposed upon its mirror image? Where is the plane of symmetry of the *eta* isomer?

12. Which should make the better solvent for *p*-dichlorobenzene, methyl or *n*-propyl alcohol?

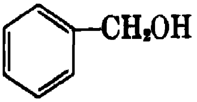
10

Hydroxy Compounds

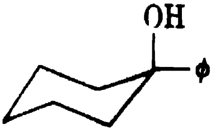
10.1 TYPES OF HYDROXY COMPOUNDS

Alcohols are aliphatic or alicyclic compounds containing one or more hydroxyl groups in their structures. Monohydric alcohols are those with one OH group per molecule; dihydric alcohols have two OH groups; and polyhydric alcohols contain many OH groups in their structures. Alcohols are classified as primary, secondary, and tertiary, depending upon whether the OH group is attached to a primary, secondary, or tertiary carbon atom, respectively. The three classes are designated by the general structures, RCH_2OH, R_2CHOH, and R_3COH.

Phenols are compounds having an OH group attached to an aromatic ring. The class name is taken from the name of the parent compound, C_6H_5OH. Other aromatic nuclei with OH groups, however, are regarded as phenols because of the similarity of their properties. If a hydroxy compound has an aromatic ring but the OH group is not attached directly to the aromatic ring, it is classed as an alcohol. For example,



and



are alcohols.

10.2 NOMENCLATURE

Under the Geneva system of naming alcohols, the ending *-e* of the corresponding alkane is replaced by *-ol*, and a numerical prefix is used to designate the position of the OH group. Alcohols can also be named under the Geneva system by regarding the OH group as a substituent on an alkane or some other class of compound. The following examples are given for illustration:

$$CH_3—CHCl—CHOH—CHCl—CH(CH_3)—CH_3$$

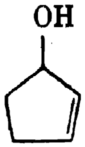
2,4-Dichloro-5-methyl-3-hexanol

or

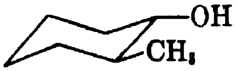
2,4-Dichloro-3-hydroxy-5-methylhexane

$$CH_3—C(CH_3)═CH—CHOH—CH_2—CH_2—CH_3$$

2-Methyl-2-heptene-4-ol
or
2-Methyl-4-hydroxy-2-heptene



Cyclopentene-3-ol
or
3-Hydroxycyclopentene



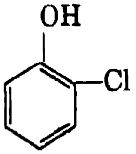
e,e-trans-2-methylcyclohexanol

Common or trivial names are used for those alcohols whose organic groups have simple names. Examples are given in Table 10.1.

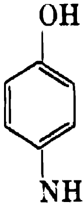
TABLE 10.1. EXAMPLES OF ALCOHOL NOMENCLATURE

Structure	*Geneva Name*	*Common Name*
CH_3OH	Methanol	Methyl alcohol or carbinol
$CH_3—CH_2OH$	Ethanol	Ethyl alcohol
$CH_3—CH_2—CH_2OH$	1-Propanol	*n*-Propyl alcohol
$CH_3—CHOH—CH_3$	2-Propanol	Isopropyl alcohol
$(CH_3)_2CH—CH_2OH$	2-Methyl-1-propanol	Isobutyl alcohol
$C_6H_5CH_2OH$	Phenylmethanol	Benzyl alcohol
$(C_6H_5)_3C—OH$	Triphenylmethanol	Triphenyl carbinol

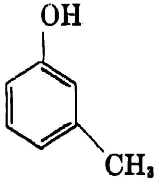
Phenols follow the aromatic scheme of nomenclature and some examples are given below:



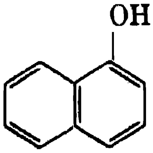
o-Chlorophenol



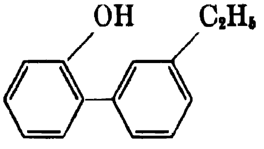
p-Aminophenol



m-Cresol



1-Naphthol



2-Hydroxy-3′-ethylbiphenyl

10.3 LABORATORY PREPARATION

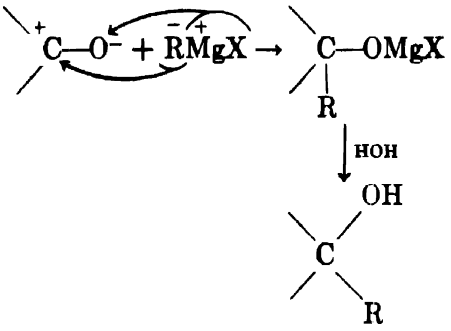
a. Alcohols. Some of the general methods of preparing alcohols may be used for all three types, primary, secondary, and tertiary, whereas other methods are unique for one type or another.

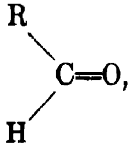
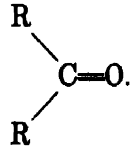
1. **Hydrolysis of alkyl halides.** The process is merely the reverse of the reaction of alcohols with halogen acids:

$$R{-}X + HOH \underset{ZnCl_2}{\overset{OH^-}{\rightleftharpoons}} R{-}OH + HX \qquad I > Br > Cl$$

Here, the equilibrium is pushed completely to the right because the HX acid is converted to the salt by reaction with the alkali. Primary, secondary, and tertiary alkyl halides yield the respective primary, secondary, and tertiary alcohols.

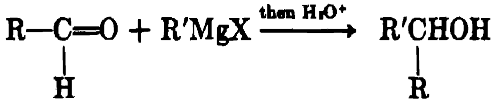
2. **Addition of Grignard reagents to carbonyl compounds.** Grignard reagents are dipolar and add in the expected direction to the polar carbonyl group.



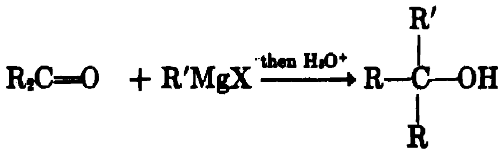
Hence, if there are two H's on the original carbonyl carbon, the product is a primary alcohol. For the preparation of secondary alcohols, one starts with one R group attached to the carbonyl group, , and for a tertiary alcohol, two R groups must be attached initially to the carbonyl group, .

Thus formaldehyde yields primary alcohols, all other aldehydes yield secondary alcohols, and ketones, $R_2C{=}O$, yield tertiary alcohols.

$$H_2C{=}O + R'MgX \xrightarrow{\text{then } H_3O^+} R'CH_2OH$$

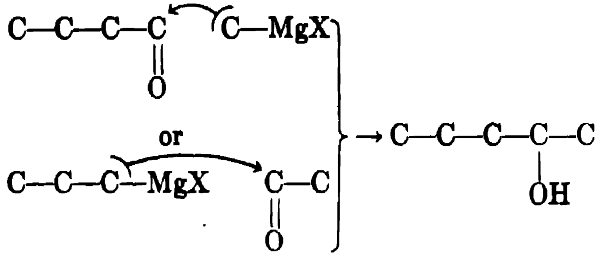


$$\underset{\displaystyle H}{R{-}C{=}O} + R'MgX \xrightarrow{\text{then } H_3O^+} \underset{\displaystyle R}{R'CHOH}$$

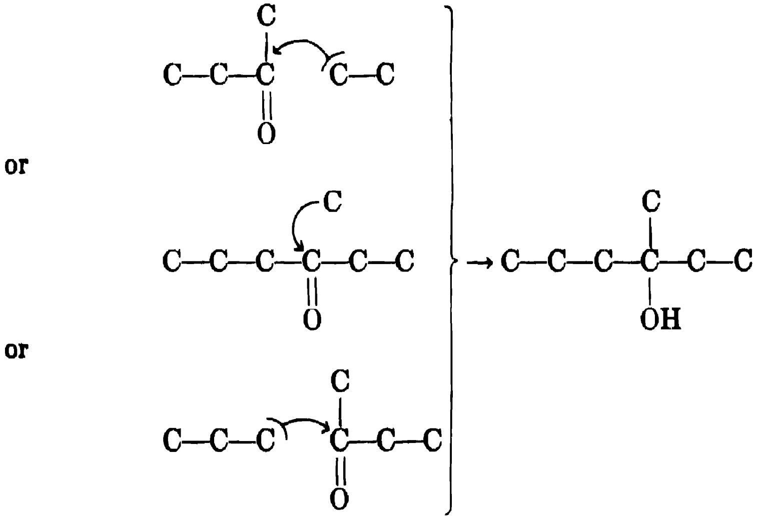


$$R_2C{=}O + R'MgX \xrightarrow{\text{then } H_3O^+} R{-}\overset{\displaystyle R'}{\underset{\displaystyle R}{C}}{-}OH$$

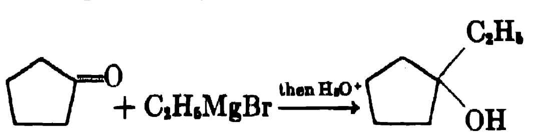
Notice that there is only one way of preparing a given primary alcohol by this reaction but that the secondary alcohol may be made by two different combinations of aldehyde and Grignard (if the R's are unlike). For illustration, 2-pentanol could be prepared by reacting butyraldehyde with a methyl Grignard or from acetaldehyde plus a propyl Grignard:



Similarly, there could be a choice from three combinations for a tertiary alcohol in which the three alkyl groups are different:

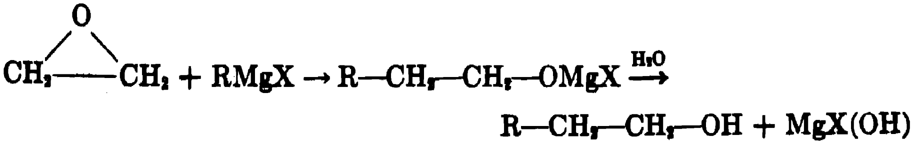


Cyclic ketones add Grignard reagents also.

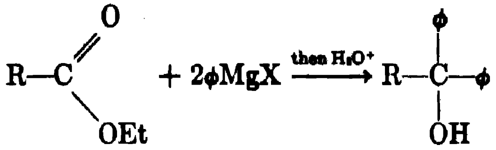


1-Ethylcyclopentanol

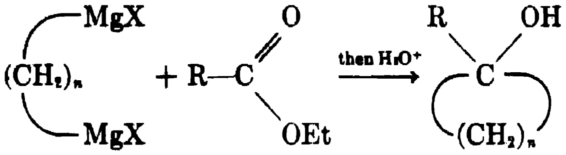
Primary alcohols may also be made by using ethylene oxide in place of formaldehyde with Grignard reagents:



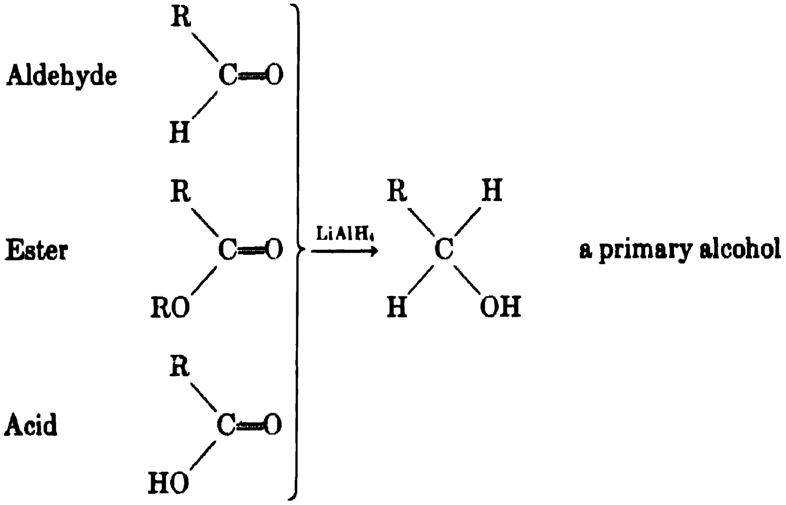
And finally, esters react with two moles of a Grignard reagent to produce tertiary alcohols:

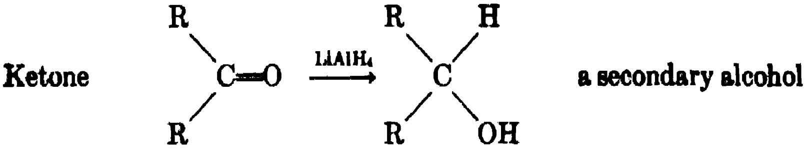


An interesting exploitation of this reaction is to use a double Grignard reagent with an ester to form a cyclic tertiary alcohol.



3. Reduction of carbonyl compounds. This method is applicable only to the preparation of primary and secondary alcohols.





Lithium aluminum hydride can be used for any of the reductions, and other familiar reducing agents are as follows:

Aldehydes and ketones $\xrightarrow{\text{R.A.}}$ Alcohols R.A. = H_2, cat.
Fe, Sn, or Zn in AcOH
NaHg
Meerwein-Ponndorf-Verley reduction (page 311)

Esters $\xrightarrow{\text{R.A.}}$ Alcohols R.A. = Na in alcohol
H_2, cat.
Zn or Sn in HCl_{aq}.

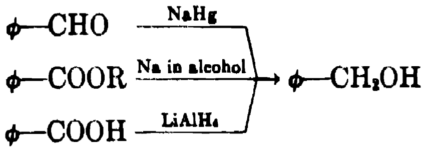
b. Arylcarbinols. Arylcarbinols are simply aryl derivatives of methanol, and other than the triarylcarbinols, have properties similar to those of aliphatic alcohols.

The benzyl alcohols are usually prepared by the general methods given above, with the additional method of hydroxymethylation.

1. Hydrolysis of benzyl halides.

$$\phi\text{—}CH_2X + KOH \rightarrow \phi\text{—}CH_2OH + KX$$

2. Reduction of aldehydes, esters, or acids.



$$\phi\text{—}CHO \xrightarrow{NaHg},\ \phi\text{—}COOR \xrightarrow{\text{Na in alcohol}},\ \phi\text{—}COOH \xrightarrow{LiAlH_4} \phi\text{—}CH_2OH$$

3. Grignard reagent plus formaldehyde.

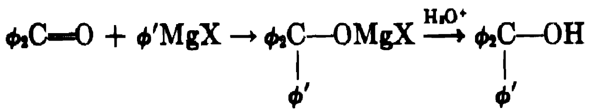
$$\phi\text{—}MgX + H_2C{=}O \rightarrow \phi\text{—}CH_2OMgX \xrightarrow{H_3O^+} \phi\text{—}CH_2OH$$

Triphenylcarbinols may be prepared by three general methods.

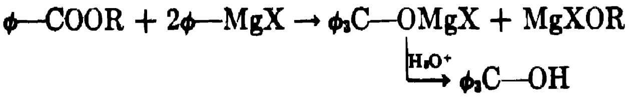
1. Hydrolysis of triphenylchloromethanes.

$$\phi_3C\text{—}X + H_2O \rightarrow \phi_3C\text{—}OH + HX$$

2. Addition of Grignards to ketones or esters.



$$\phi_2C{=}O + \phi'MgX \rightarrow \underset{\phi'}{\phi_2\overset{}{C}}\text{—}OMgX \xrightarrow{H_3O^+} \underset{\phi'}{\phi_2C}\text{—}OH$$



$$\phi\text{—}COOR + 2\phi\text{—}MgX \rightarrow \phi_3C\text{—}OMgX + MgXOR \xrightarrow{H_3O^+} \phi_3C\text{—}OH$$

3. Oxidation of triphenylmethanes.

$$\phi_3C\text{—}H \xrightarrow{PbO_2} \phi_3C\text{—}OH$$

This oxidation is atypical for aliphatic C—H bonds, but the presence of the three phenyl groups activates the C—H bond to facilitate the oxidation.

Triphenylcarbinols behave as weak bases in concentrated sulfuric acid to yield carbonium ions (cf. page 272).

$$\phi_3C\text{—}OH + 2H_2SO_4 \rightleftharpoons \phi_3C^+ + H_3O^+ + 2HSO_4^-$$

c. Phenols. The laboratory preparation of phenols is through the diazotization of anilines.

$$\phi\text{—NH}_2 + \text{HCl} + \text{NaNO}_2 \rightarrow \phi\text{—OH} + \text{N}_2 + \text{H}_2\text{O} + \text{NaCl}$$

This is merely the over-all reaction, and more will be said about the reaction in Section 16.1d.

10.4 INDUSTRIAL PREPARATIONS

The most general methods used in the commercial production of hydroxy compounds involve large-scale adaptations of the laboratory methods given above. Nothing special need be said about these processes; instead, some of the specialized commercial productions will be discussed briefly.

a. Methyl alcohol. The principal source of methanol until World War II was wood, for which reason it became known as *wood alcohol.*

When wood is heated in a vessel at temperatures around 400°, gases, a liquid condensate, and charcoal are produced. The liquid condensate separates into an aqueous phase, called *pyroligneous acid,* and a tarry layer. The pyroligneous acid is mostly water but contains close to 5% methyl alcohol, 5–10% acetic acid, 0.5% acetone, and smaller amounts of other organic substances. Today over 90 per cent of methyl alcohol production is from the catalytic hydrogenation of carbon monoxide obtained from natural gas at elevated temperatures and pressures.

$$\text{CH}_4 \xrightarrow{\text{O}_2} \text{CO} + \text{H}_2 \xrightarrow[350^\circ]{\text{ZnO—Cr}_2\text{O}_3} \text{CH}_3\text{OH}$$

b. Ethyl alcohol. Ethanol, commonly called *grain alcohol,* and in former days known as *spirits of wine,* has been known and used since the dawn of history, principally in the form of fermented beverages. Ancient peoples knew how to recover the intoxicating principle from such beverages by a crude form of distillation. Originally, the alcohol was recovered as dilute, impure solutions from fermented fruit or grain, hence, the origin of the earlier names.

Many substances may be fermented, yielding alcohol and other organic compounds, and each raw material imparts a distinct flavor to the product. Thus, *brandy* is the distillate from fermented fruit; *rum* is distilled from molasses; *Bourbon whisky* from corn, *rye whisky* from rye, *Scotch whisky* from barley, *Irish whisky* from potatoes, *saki* from rice, and *beer* from malt to which the flower of the hop plant has been added to produce a bitter taste. Molasses has become an important raw material for the production of other substances by fermentation, such as antibiotics, pharmaceuticals, and many chemical intermediates.

Over 75 per cent of commercial-grade ethyl alcohol is produced today by hydration of ethylene.

$$\text{CH}_2\text{=CH}_2 + \text{HOH} \xrightarrow{\text{H}_2\text{SO}_4} \text{CH}_3\text{CH}_2\text{OH}$$

Twenty years ago the situation was reversed, and 75 per cent of all ethyl alcohol was produced by the fermentation of molasses. Now less than 25 per cent comes from the fermentation of carbohydrates. Three types of raw materials are used for this production of ethyl alcohol:

1. Molasses, which is the mother liquor from the extraction and crystallization of sugar from sugar cane, and which has an approximate 55 per cent sugar content. This is imported chiefly from Puerto Rico.
2. Starch from grains, such as wheat, corn, barley, etc. The chief source of starch in the United States is corn; in Europe, potatoes; and in Asia, rice.
3. Cellulose from wood pulp. For the latter, the fermentation plant is located near a sawmill in order to use the waste sawdust as the raw material.

Wood has a high cellulose (page 555) content, and in 1928, the German chemist Scholler perfected a process for converting wood cellulose into sugar by acid hydrolysis. The sugar obtained from any one of these three sources is then fermented to produce ethyl alcohol (see Fig. 10.1). The fermented liquor or "wort," which contains 6–10 per cent ethyl alcohol and other compounds, is fractionated into three fractions: (1) first cut, consisting mainly of acetaldehyde, CH_3CHO; (2) *rectified spirit*, which is 93–95 per cent ethanol by weight; (3) final cut or *fusel oil*, which contains propyl, butyl, and pentyl alcohols.

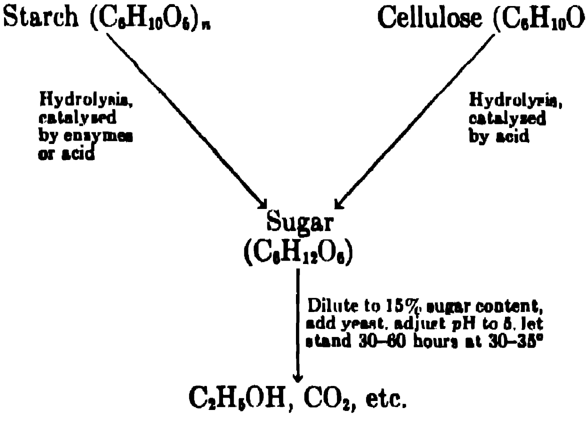

Starch $(C_6H_{10}O_5)_n$
Cellulose $(C_6H_{10}O_5)_n$
Hydrolysis, catalysed by enzymes or acid
Hydrolysis, catalyzed by acid
Sugar $(C_6H_{12}O_6)$
Dilute to 15% sugar content, add yeast, adjust pH to 5, let stand 30–60 hours at 30–35°
C_2H_5OH, CO_2, etc.

Fig. 10.1

Lastly, a small amount of ethyl alcohol is formed as a side product in the synthetic liquid fuel industry (see Section 2.9).

There are three grades of ethyl alcohol commonly sold. The one which is purified by fractional distillation has a 93–95 per cent alcohol content by weight, and is called *commercial grade*. For several centuries it has been customary for governments to levy a tax on alcoholic solutions and distillates, thus raising revenue while penalizing those who use intoxicating beverages containing alcohol.

In recent years an unprecedented amount of attention has been paid to the drinking of alcohol and the problems arising therefrom. The major benefit has been to shift the disease of alcohol addiction out of the realm of morals into the sphere of psychiatry and medicine.

When a person swallows some liquor, his stomach receives a certain amount of pure ethyl alcohol. The alcohol goes from the stomach to the liver, then on to the heart, from where it is pumped throughout all parts of the body. As a person drinks more, the concentration of alcohol in the body fluids increases. Effects of this alcohol—slurred speech, double vision, incoordination—are the result of disturbed brain activity. Alcohol does not damage brain tissue but merely slows down the brain's functions. First it attacks the brain area containing centers of judgment and inhibition. Then when the alcohol concentration in body fluids rises, it attacks muscular coordination, speech, and vision. Finally, at a concentration of about 10 oz of alcohol per 150 lb body weight, all voluntary control is lost and man loses consciousness.

The amount of liquor a person can drink and still remain sober depends on how slowly he drinks. If an average-sized man were to drink a pint of 86-proof liquor in 4 hrs, which contains 6.9 oz of actual alcohol, only 5 oz would accumulate in body fluids (13 gal, including 6–7 qt of blood). The rest is burned and eliminated. There is a close relationship between the concentration of alcohol in the blood and that in the urine, the breath, the spinal fluid, and the saliva. Police tests for intoxication are usually based upon one of these, most often that in the breath.

In brief, alcohol is an easily controlled brain anesthetic. The evils of alcoholism are not due to physical damage to the body, which is negligible, but to the widely recognized social disturbances it causes. Rather than the alcoholic, it is his family or friends that suffer most. Of the estimated 50 million users of alcohol in the United States, about 46 million are purely "social drinkers" and offer no problem. Three million others are "excessive drinkers" who like to get drunk occasionally at social gatherings or celebrations, but who for the rest of the time handle alcohol carefully and may not drink at all. Finally, there are the 750,000 alcohol addicts who drink for a wide variety of reasons. There are several treatments given alcoholics, the more recent ones leaning toward some form of psychiatry or diet control. The average of cures reported for all treatments now in use is said to be above 50 per cent, compared to 20 per cent in 1930.

When alcohol is used in manufacturing operations, the tax, of course, would be absorbed in the final retail price to the public. To avoid unnecessarily high consumer prices, the U.S. Congress in 1906 passed an act permitting the sale of tax-free denatured alcohol for industrial purposes. *Denatured alcohol* is merely alcohol which has been rendered unfit for human consumption by the addition of other substances. Any one of several additives may be used, such as wood alcohol, foul-smelling substances, etc. An additive is chosen which does not interfere with the chemical function of the alcohol.

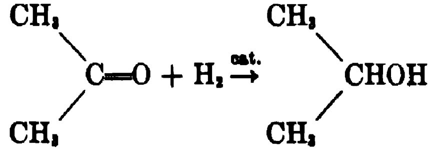
The third grade of alcohol commercially available is *absolute alcohol*, or 100 per cent pure alcohol. Alcohol and water form a minimum boiling azeotrope of 95 per cent alcohol content. Hence, when a dilute aqueous solution of alcohol is fractionally distilled, the highest concentration of alcohol obtainable is 95 per cent. To prepare pure alcohol in the laboratory, one treats the 95 per cent material with a drying agent like calcium oxide to adsorb the water; then the dry alcohol is distilled. Commercially, absolute alcohol is obtained by codistillation of 95 per cent material with benzene, C_6H_6. Ethanol, benzene, and water form a minimum-boiling, 3-component azeotrope (18.5 per cent alcohol, 74.1 per cent benzene, 7.4 per cent water) which boils at 65°. Sufficient benzene is added to distill this tertiary azeotrope untill all the water has been removed. Then, benzene and alcohol form a binary azeotrope (80 per cent benzene, 20 per cent alcohol) which boils at 68°, and this distills until all the benzene is carried over, leaving only alcohol behind. Such a procedure uses up too much alcohol for a laboratory method, and therefore is only feasible for industrial plants where the alcohol passing over in the mixtures can be poured back into the still for the next day's run.

In Section 3.2b was mentioned the commercial production of ethylene from ethanol, and here, ethylene is being used to produce ethanol. The key to this situation is the difficulty and expense of transporting ethylene because of its gaseous condition and light weight. The same circumstance is true for natural gas. For example, in the Northwest the United States exports natural gas to Canada, and in the Northeast it imports natural gas from Canada. In an area where ethylene has little value, it is profitable to convert it to ethanol, ship the ethanol to a locality where ethylene is needed but not readily available, and then dehydrate the ethanol to ethylene.

c. Propyl alcohols. *n*-Propyl alcohol is also produced by the catalytic hydrogenation of carbon monoxide, but with a different catalyst from that used in the production of methyl alcohol. It is also produced by the hydration of propene.

$$CH_3{-}CH{=}CH_2 + HOH \xrightarrow{\text{abnormal addition}} CH_3{-}CH_2{-}CH_2OH$$

Isopropyl alcohol is produced by the normal hydration of propene and by the hydrogenation of acetone.



$$(CH_3)_2C{=}O + H_2 \xrightarrow{\text{cat.}} (CH_3)_2CHOH$$

d. Phenol. The commercial preparation of phenols has generally been through the hydrolysis of aryl halides.

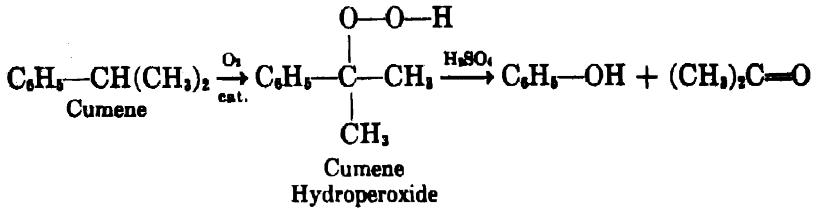
$$\phi{-}X + Na_2CO_3 + H_2O \xrightarrow[\Delta]{325°} \phi{-}OH + NaX + NaHCO_3$$

A new Dow Chemical Company process shows promise of supplanting this method by one involving the oxidation of alkylbenzenes.

$$\phi{-}R \xrightarrow[\text{cat.}]{\text{air}} \phi{-}COOH \xrightarrow[\text{cat.}]{\text{air}} \phi{-}OH + CO_2$$

The hydroxyl group becomes attached to the ring at a position adjacent to the departing carboxyl group.

In the past, unsubstituted phenol has been produced by the hydrolysis of chlorobenzene, the alkali fusion of sodium benzenesulfonate, and from coal tar. Phenol is synthesized now largely by Dow's cumene process.



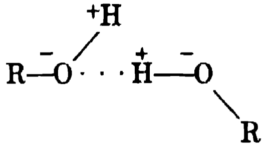
$$C_6H_5{-}CH(CH_3)_2 \xrightarrow[cat.]{O_2} C_6H_5{-}\overset{\overset{O-O-H}{|}}{\underset{\underset{CH_3}{|}}{C}}{-}CH_3 \xrightarrow{H_2SO_4} C_6H_5{-}OH + (CH_3)_2C{=}O$$

Thus, the cumene process also serves as an additional source of acetone.

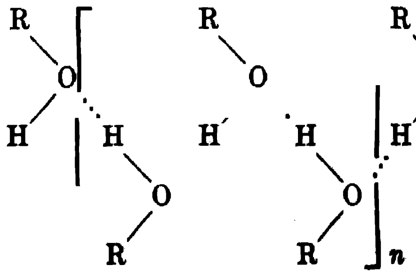
10.5 PHYSICAL PROPERTIES AND HYDROGEN BONDING

The most prominent physical property of hydroxy compounds is their association through hydrogen bonds. It is appropriate, therefore, to discuss hydrogen bonds in general.

It was shown in Section 1.2 that covalent bonds may have a partial ionic character owing to differences in electronegativities of the two atoms forming the covalent bond. Whenever hydrogen is bonded to one of the highly electronegative atoms, such as oxygen or nitrogen, the bond has a considerable ionic nature, with the hydrogen atom carrying a partial positive charge. Thus, it has a coulombic attraction for a negatively charged atom. At the same time, the other atom of the covalent bond with hydrogen carries a fractional negative charge. Thus, with a hydroxylic compound, the hydrogen atom of one OH group is attracted to the oxygen atom of a second OH group.



This attraction weakly binds two molecules together. Weak cohesion of molecules is called *association*, and in this case it is due to hydrogen bridges between molecules. The weak electrostatic portion of the hydrogen bridge is conventionally designated by *dots*, and the stronger, more covalent portion by the usual *dash*. Therefore, the association of alcohol molecules to form large aggregates, primarily in the liquid and solid states, is diagramed as follows:



where R represents an alkyl group and n is an indefinite number. In such a condition, a substance is referred to as being *associated.*

The boiling point is the temperature at which thermal agitation of molecules is sufficient to overcome the attractive forces between them in the liquid state. It is logical to expect the boiling point to be higher for heavier molecules and with stronger intermolecular forces. Alkane molecules have extremely weak intermolecular forces of attraction, and their boiling points are taken as references for given molecular weights. They are spoken of as having *normal* boiling points. In Table 10.2 it can be seen that the boiling points of ethers and alkanes of comparable molecular weights are not far apart, but that the boiling points of alcohols with equivalent molecular weights are considerably higher. The alcohol molecules are held together by hydrogen bonds, and it requires more energy to separate them for vaporization.

TABLE 10.2. BOILING POINTS OF *n*-ALKANES, ETHERS, AND ALCOHOLS OF COMPARABLE MOLECULAR WEIGHTS

n-Alkanes	B.P.	Ethers	B.P.	Alcohols	B.P
$CH_3—CH_2—CH_3$	−45°	$CH_3—O—CH_3$	−25°	$CH_3—CH_2—OH$	78°
$CH_3CH_2CH_2CH_3$	−0.5	$CH_3—O—CH_2CH_3$	8	$CH_3CH_2CH_2OH$	97
$CH_3(CH_2)_3CH_3$	36	$CH_3CH_2—O—CH_2CH_3$	35	$CH_3(CH_2)_2CH_2OH$	118
$CH_3(CH_2)_4CH_3$	69	$CH_3CH_2—O—CH_2CH_2CH_3$	61	$CH_3(CH_2)_3CH_2OH$	138

Another illustration (see Table 10.3) of the effect of hydrogen bonding on boiling points is found in a comparison of the boiling points of polyhydric alcohols and their ethers.

TABLE 10.3. BOILING POINTS OF POLYHYDRIC ALCOHOLS AND THEIR ETHERS

$\begin{array}{l}CH_2OH\\ \vert\\ CHOH\\ \vert\\ CH_2OH\end{array}$	$\begin{array}{l}CH_2OC_2H_5\\ \vert\\ CHOH\\ \vert\\ CH_2OH\end{array}$	$\begin{array}{l}CH_2OC_2H_5\\ \vert\\ CHOH\\ \vert\\ CH_2OC_2H_5\end{array}$	$\begin{array}{l}CH_2OC_2H_5\\ \vert\\ CHOC_2H_5\\ \vert\\ CH_2OC_2H_5\end{array}$
B.p. = 290°	230°	191°	185°
	$\begin{array}{l}CH_2OH\\ \vert\\ CH_2OH\end{array}$	$\begin{array}{l}CH_2OCH_3\\ \vert\\ CH_2OH\end{array}$	$\begin{array}{l}CH_2OCH_3\\ \vert\\ CH_2OCH_3\end{array}$
	B.p. = 197°	125°	84°

In both series, as the OH groups are successively covered by alkyl groups to block hydrogen bonding, the boiling points progressively decrease in spite of the increases in molecular weights.

Sulfur is much less electronegative than oxygen, which causes S—H bonds to have much smaller ionic character than O—H bonds. Accordingly, compounds having S—H groups in their structures do not exhibit hydrogen bonding to any significant extent. For illustration, the boiling points of OH compounds are higher than those of corresponding SH compounds:

Boiling Points of Some —OH and —SH Compounds

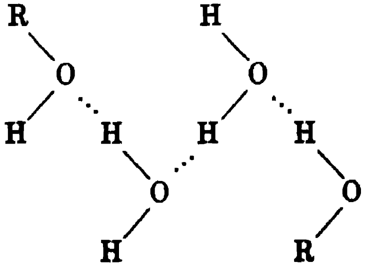
HOH	100°	−62°	HSH
CH_3OH	66	6	CH_3SH
CH_3COOH	119	93	CH_3COSH

That this is due to stronger hydrogen bonding occurring in OH compounds is shown by the fact that sulfur compounds, because of their larger molecular weights, ordinarily have higher boiling points than the oxygen compounds when hydrogen bonding cannot occur. Two illustrations are

$(CH_3)_2O$	−24°	38°	$(CH_3)_2S$
$(C_2H_5)_2O$	35	92	$(C_2H_5)_2S$

Hydrogen bonds, then, are weak electrostatic bonds involving a hydrogen bridge between two atoms. The bond may be *inter*molecular (between two atoms of different molecules), or *intra*molecular (between two atoms within the same molecule). Hydrogen bonds are only about one-tenth as strong as typical covalent and ionic bonds. Nevertheless, hydrogen bonds have very marked effects upon the physical properties of compounds.[1] For example, the acid strength, color, boiling point, adsorption affinity, and water solubility are just some of the properties found to be profoundly affected by hydrogen bonding. Also, hydrogen bonds are key factors in certain commercial processes, such as dyeing of fabrics and the action of nonionic detergents.

Water is a highly associated liquid, as evidenced by its relatively high boiling point for such a low-molecular-weight compound. The OH group of water may also form a hydrogen bond with the OH group of an alcohol molecule when mixed, and conversely, the OH group of an alcohol molecule may form a hydrogen bond with an OH group of water:



Such coassociation tends to make hydroxylic compounds soluble, and indeed, methyl, ethyl, propyl alcohols and others are soluble in water in all propor-

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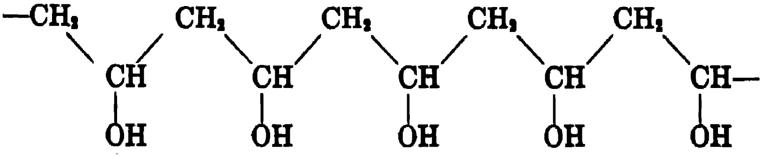
[1] L. N. Ferguson, *J. Chem. Educ.*, 33, 267 (1956).

TABLE 10.4. PHYSICAL CONSTANTS OF SOME ALCOHOLS AND PHENOLS

Name	Melting Point	Boiling Point	Solubility (g/100g H_2O)
Methyl alcohol	−97	64.5	∞
Ethyl alcohol	−115	78.3	∞
n-Propyl alcohol	−126	97	∞
n-Butyl alcohol	−90	118	7.9
n-Pentyl alcohol	−79	138	2.3
n-Hexyl alcohol	−52	157	0.6
n-Heptyl alcohol	−34	176	0.2
n-Octyl alcohol	−15	195	0.05
Isopropyl alcohol	−86	82.5	∞
Isobutyl alcohol	−108	108	10
sec-Butyl alcohol	−114	99.5	12.5
tert-Butyl alcohol	26	83	∞
Allyl alcohol	−129	97	∞
Cyclopentanol		140	
Cyclohexanol	−24	162	
Benzyl alcohol	−15	205	4
Phenol	41	182	9.3
Hydroquinone	173	286	8

	Ortho		*Meta*		*Para*	
	M.P.	B.P.	M.P.	B.P.	M.P.	B.P.
Cresol	31	191	11	201	35	202
Fluorophenol	16	152	14	178	48	185
Chlorophenol	9	173	33	214	43	220
Bromophenol	5	194	33	236	64	236
Aminophenol		174	123		186	
Nitrophenol	45	217	96		114	
Dihydroxybenzene	104	246	110	281	169	286

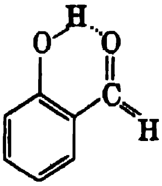
tions (cf. Table 10.4). The hydrocarbon portion of an alcohol, of course, resists entering into water solution and when it becomes large, the solubilizing effect of hydrogen bonding is outweighed and the alcohol is no longer water soluble. However, when there is a large ratio of OH groups to hydrocarbon groups, a compound will have a significant solubility in water. For example, polyvinyl alcohol, a polymer of large molecular weight,



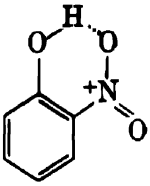
is quite soluble in water.

Phenols are moderately soluble in water, owing to association through hydrogen bonds. Nevertheless, at room temperature the solubilities are too low to use water as a solvent for reactions. Hence, one normally expects phenols to form separate phases with water.

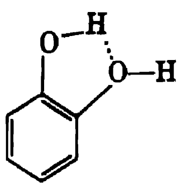
So far, we have seen that *intermolecular* hydrogen bonds increase transition temperatures and water solubility of a compound. *Intramolecular* hydrogen bonds have the opposite effect and tend to make the compound behave as if it did not have a hydroxyl group present. Intramolecular hydrogen bonds are formed between OH groups and neighboring C═O, NO_2, or even other OH groups. Thus, the *ortho* isomers of hydroxybenzaldehyde or nitrophenols melt at lower temperatures than the *para* isomers (cf. Table 10.5).



Salicylaldehyde



o-Nitrophenol



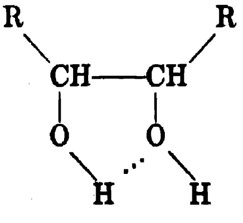
Catechol

This accounts for the fact that the solubilities of *o*- and *p*-nitrophenols in 100 ml of boiling water are 1 g and 27 g, respectively, and the fact that salicylaldehyde is only slightly soluble in hot water, whereas *p*-hydroxybenzaldehyde is soluble. Intramolecular hydrogen bonds tie up the OH groups and prevent them from associating with water through intermolecular hydrogen bonds.

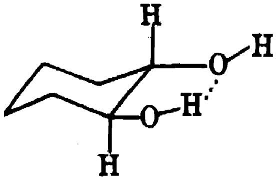
TABLE 10.5. MELTING POINTS OF SOME ISOMERIC BENZENES

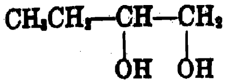
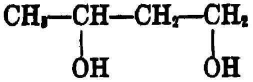
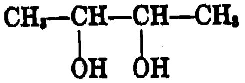
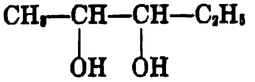
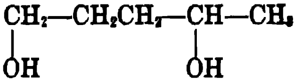
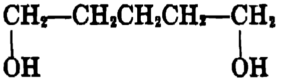
	Melting Points	
Compound	*ortho Isomer*	*para Isomer*
Nitrophenol	44°	114°
Hydroxybenzaldehyde	−7°	116°
Dihydroxybenzene	104°	169°

Adjacent OH groups form five-membered rings through hydrogen bonds and this lowers the boiling point.



and



1,2-Diols	*B.P.*	*Other Isomers*	*B.P.*
 $CH_3CH_2-\underset{OH}{\underset{\mid}{CH}}-\underset{OH}{\underset{\mid}{CH_2}}$	191°	 $CH_3-\underset{OH}{\underset{\mid}{CH}}-CH_2-\underset{OH}{\underset{\mid}{CH_2}}$	203°
 $CH_3-\underset{OH}{\underset{\mid}{CH}}-\underset{OH}{\underset{\mid}{CH}}-CH_3$	183°		
 $CH_3-\underset{OH}{\underset{\mid}{CH}}-\underset{OH}{\underset{\mid}{CH}}-C_2H_5$	188°	 $\underset{OH}{\underset{\mid}{CH_2}}-CH_2CH_2-\underset{OH}{\underset{\mid}{CH}}-CH_3$	219°
		 $\underset{OH}{\underset{\mid}{CH_2}}-CH_2CH_2CH_2-\underset{OH}{\underset{\mid}{CH_2}}$	238°

Spectroscopic properties are markedly affected by hydrogen bonding, and this has been the most powerful method of studying hydrogen bonds. The infrared absorption frequencies associated with the stretching of O—H or C=O bonds are smaller when these groups are involved in a hydrogen bond. That is, the H bridge makes it easier for the bond stretching to take place and less energy, i.e., lower frequency of light, is needed to produce the atomic vibrations. Some examples are given below.

Normal

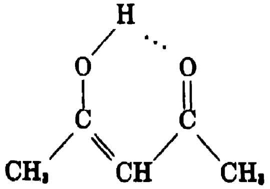
$(CH_3)_3C-OH$

$\nu_{O-H} = 3610\ cm^{-1}$

$(CH_3)_2C=O$

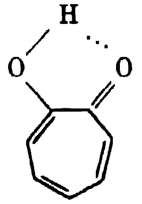
$\nu_{C=O} = 1726\ cm^{-1}$

Hydrogen bonded

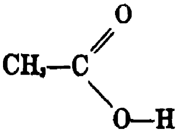


$\nu_{O-H} = 2800\ cm^{-1}$

$\nu_{C=O} = 1610\ cm^{-1}$

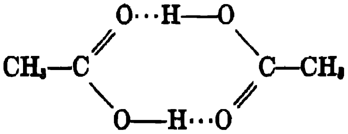


$\nu_{C=O} = 1597\ cm^{-1}$



$\nu_{O-H} = 3521\ cm^{-1}$

$\nu_{C=O} = 1768\ cm^{-1}$



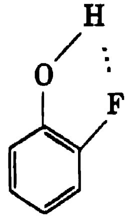
$\nu_{O-H} = 3073\ cm^{-1}$

$\nu_{C=O} = 1701\ cm^{-1}$

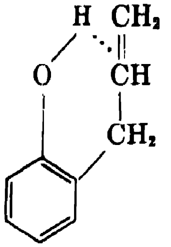
Notice that *intra-* as well as *inter*molecular hydrogen bonds produce this lowering of the normal frequencies. One can distinguish intermolecular hydrogen bonding from intramolecular by studying solvent, temperature, or concentration effects on the ν_{OH} frequencies.

Emphasis has been placed here on O—H···O hydrogen bonds, but H bridges are formed between other highly electronegative atoms as well, e.g., O—H···N, N—H···N, O—H···X, where X is a halogen atom, and including carbon atoms when their electronegativities are increased by having several other highly electronegative atoms attached. Thus, there are intermolecular C—H···Cl bonds between $CHCl_3$ molecules in chloroform, and intramolecular O—H···F bonds in *o*-fluorophenol.

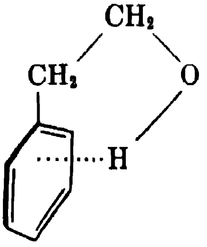
$Cl_3C—H \cdots Cl—CHCl_2$



Also, hydrogen bonds can be formed with π electrons. Such bonds, for example, occur in *o*-allylphenol, β-phenylethanol, and *o*-hydroxybiphenyl.



o-Allylphenol



β-Phenylethanol

free $\nu_{OH} = 3605\ cm^{-1}$

$\nu_{O-H\cdots\pi} = 3542\ cm^{-1}$

intermol. $\nu_{O-H\cdots O} = 3360\ cm^{-1}$

free $\nu_{O-H} = 3630\ cm^{-1}$

$\nu_{O-H\cdots\pi} = 3601\ cm^{-1}$

Throughout the text so far, mention has been made of the attraction of molecules for one another through weak forces. These forces are of three types which differ in magnitude and effective range.

Van der Waals Attraction.[2] Although the negative charges of the electrons in a neutral molecule are balanced by the positive charges on the nuclei, the electrons are in constant motion, and the center of density of the negative charges (i.e., a point which may be regarded as the time-average position for all of the negative charges) does not coincide continuously with the center of density of the positive charges. This situation produces small local dipoles; that is, areas with a positive and negative end and which behave as small electric magnets. When molecules are close enough, these dipoles attract each other like magnetic bars, causing the molecules to cling to one another. Such attraction is called *van der Waals attraction*, and the greater the area over which molecules may come in close contact, the greater is the over-all van der Waals force. For straight-chain hydrocarbons, the forces are about 1.0 kcal per CH_2

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[2] J. D. van der Waals, a Dutch physical chemist, received the Nobel Award in physics in 1910.

unit, which explains the regular increase in boiling point with increasing chain length within a homologous series. Branching of a chain decreases the area over which a molecule may "touch" other molecules, and accordingly, the boiling points of isomers decrease with the degree of branching. For example, the boiling points of normal, iso-, secondary-, and tertiary-butyl alcohols are 117°, 107°, 100°, and 83°, respectively. Van der Waals forces become weaker in proportion to the seventh power of the distance between molecules, $F \alpha 1/d^7$. A short separation of molecules markedly decreases the van der Waals force of attraction and, hence, they are effective for only short intermolecular distances, or in other words, they are very short-range forces.

Dipole Association. The dipoles which arise from the unequal sharing of electrons by covalently bonded atoms are referred to as *bond dipoles*, and their magnitudes are indicated by the size of their *bond moments* (Table 10.6). Bond dipoles in different molecules attract one another and such attraction is called *dipole-dipole attraction*. Dipole-dipole forces vary inversely as the fourth power of the distance between molecules, $F \alpha 1/d^4$. Thus, they too are effective only for short distances, but are of longer range than van der Waals forces. The effects of dipole association are the same as from hydrogen bonding, only to a smaller extent. Thus, compounds made up of bonds having large bond dipoles are somewhat polar. This is reflected in those properties which involve the separation of molecules, such as boiling points and heats of vaporization. The greater the association, the greater is the energy required to separate molecules for vaporization (Table 10.7). Now, related to heats of vaporization is Trouton's constant. This is the ratio of the molar heat of vaporization to the absolute boiling point of a substance. This constant is found to be a useful index for the relative polarity of organic compounds (see Table 10.7). Knowledge of the relative polarity of organic compounds is of particular value when seeking a solvent for a substance. One looks among the polar liquids, i.e., alcohols and acids, for a solvent for a polar compound, and among the nonpolar liquids for a solvent for a nonpolar substance.

TABLE 10.6. BOND MOMENTS OF SOME COMMON BONDS

Bond (+ −)	Moment e.s.u. × 10^8	Bond (+ −)	Moment e.s.u. × 10^8
H—F	1.91	C—F	1.51
H—O	1.53	C—Cl	1.56
H—N	1.31	C—Br	1.48
H—Cl	1.08	C—I	1.29
H—Br	0.79	C—S	0.95
H—S	0.68	C—N	0.45
H—I	0.42	C═N	0.90
H—C	0.30	C—O	0.85
		C═O	2.50

Hydrogen-bond Forces. Hydrogen, owing to its small size and rather low electronegativity, is unique in the fact that it forms hydrogen bonds, as discussed above. Excluding one or two exceptional cases, hydrogen-bond strengths are in the range 2–8 kcal, which is small in comparison to 80 kcal for a C—C covalent bond or to 125 kcal for the ionic attraction between a K^+Cl^- ion pair. As was observed above, however, they are sufficiently strong to produce significant effects upon the properties of substances.

TABLE 10.7. SOME PROPERTIES REFLECTING POLAR CHARACTER OF VARIOUS CLASSES OF COMPOUNDS OF COMPARABLE MOLECULAR WEIGHTS

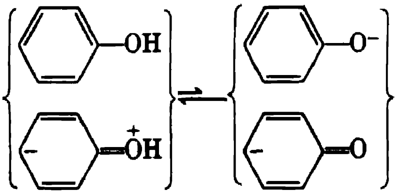
Compound	Class	Mol. Wt.	B.P.	Heat of Vaporization (kcal./mole)	Trouton's Constant
$CH_3CH_2CH_2CH_3$	Alkane	58	−0.6°	5.3	19.4
CH_3CH_2Cl	Alkyl chloride	64.5	13	6.0	20.5
$(CH_3CH_2)_2O$	Ether	74	34.6	6.2	20.2
$CH_3—COCl$	Acid chloride	78.5	52	6.2	21.5
$CH_3—CO—CH_3$	Ketone	58	56	7.2	21.9
$CH_3—COOCH_3$	Ester	74	57.5	7.3	22.1
CH_3CH_2CN	Nitrile	55	97	7.4	20
CH_3NO_2	Nitroalkane	61	99.9	8.2	22.1
$CH_3CH_2CH_2OH$	Alcohol	60	98	9.9	26.6
CH_3COOH	Carboxylic acid	60	118	11.6	29.6
$CH_3—CONH_2$	Amide	59	222		

Another important physical property of some of the hydroxy compounds is their acidity. Phenols are weak acids, generally with K_a values about 10^{-10}.

The greater acid strength of phenols over that of alcohols can be explained in terms of resonance.

$$ROH \rightleftharpoons RO^- + H^+ \qquad K_a \simeq 10^{-16}$$

Only one structure each need be written for the alcohol and its ion in order to account for their properties; hence, resonance stabilization of each is nil. Thus, resonance has no detectable effect on the position of equilibrium. For the dissociation of a phenol,



$+ H^+ \qquad K_a = 10^{-10}$

resonance occurs for the phenol and its ion. Resonance of the phenol places a positive charge on the oxygen atom, thereby facilitating escape of the proton. Also, resonance of the ion is greater than that of the acid form, because charge-separation diminishes the stability, i.e., decreases the importance of the ionic resonance form of the acid. Therefore, resonance stabilization is greater for the ion than for the acid. This net resonance stabilization of the ion, and the charge effect of resonance in the acid lead to greater dissociation of phenols than occurs for alcohols.

Particularly when *ortho* or *para* to the *OH* group, *m*-directing groups are acid-strengthening. For instance, the K_a's of phenol and nitrophenols are as follows:

	K_a
Phenol	1.3×10^{-10}
p-Nitrophenol	6.9×10^{-8}
2,4-Dinitrophenol	1×10^{-4}
2,4,6-Trinitrophenol (picric acid)	4.2×10^{-1}

Thus, picric acid is a strong acid. Without this group-activating effect, phenols are acidic enough to dissolve in aq. Na_2CO_3, but not in aq. $NaHCO_3$.

10.6 CHEMICAL PROPERTIES OF HYDROXY COMPOUNDS

One view is to regard an alcohol as a monoalkyl derivative of water. In this connection the lower alcohols resemble water in some ways. For example, the association of alcohols and water has already been discussed. Alcohols also form solvates with inorganic salts just as water does. Those with water are called *hydrates*, and those with alcohols are called *alcoholates*. For instance, there are calcium chloride triethanolate, $CaCl_2 \cdot 3C_2H_5OH$, and copper sulfate dimethanolate, $CuSO_4 \cdot 2CH_3OH$. Other similarities between water and alcohols will become apparent as the chemical properties of alcohols are discussed.

If ethanol and a saturated water solution of calcium acetate are mixed, the mixture rapidly solidifies to a gel. The excess liquid may be squeezed out and the gel ignited. A commercial application of this, sometimes called *canned heat*, or *Sterno*, is used by campers as a source of heat.

Alcohols undergo some reactions through the hydroxylic hydrogen atom, and they undergo other reactions in which the entire OH group is replaced. In the former case, the order of decreasing reactivity is primary, secondary, tertiary. Three such reactions are the replacement of the hydroxylic hydrogen atom by (1) an active metal, (2) an alkyl group, and (3) by an acyl group.

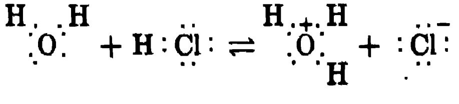
a. Formation of alkoxides. $ROH + Na \rightarrow RONa + \frac{1}{2}H_2$. The product, RONa, is a sodium alkoxide, whose specific name depends upon the structure of the R group. Thus, CH_3ONa is sodium methoxide, $(CH_3)_2CHONa$ is sodium isopropoxide, and C_6H_5ONa is sodium phenoxide. Alkoxides and phenoxides are white, powdery, deliquescent materials, soluble in alcohols, and hydrolyzed rapidly in water.

$$RONa + HOH \rightleftharpoons ROH + NaOH$$

The equilibrium for this reaction lies far to the right, indicating that either (1) RONa is a stronger base than NaOH, or (2) HOH is a stronger acid than ROH, or both (1) and (2). Actually (1) and (2) are both true.

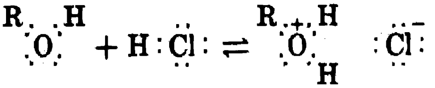
The reaction of sodium metal with alcohols is not as vigorous as with water and offers a means of destroying waste sodium metal. Usually a large excess of methyl or ethyl alcohol is poured on the waste sodium and allowed to stand until all evidence of reaction has ceased. The mixture may then be discarded. Other metals react with alcohols, too, but more slowly than the alkali metals. Magnesium and calcium react slowly with anhydrous alcohols, and aluminum is usually amalgamated for reaction with alcohols.

Hydronium ions are formed when a strong acid is dissolved in water.



$$\underset{\cdot\cdot}{\overset{H\cdot\ \cdot H}{:O:}} + H:\underset{\cdot\cdot}{\overset{\cdot\cdot}{Cl}}: \rightleftharpoons \underset{H}{\overset{H\cdot+\cdot H}{:O:}} + :\underset{\cdot\cdot}{\overset{\cdot\cdot\,-}{Cl}}:$$

Thus water is more basic than the chloride ion and takes the proton away from the chloride ion. An alcohol molecule is also basic, and will form an oxonium ion with a strong acid.



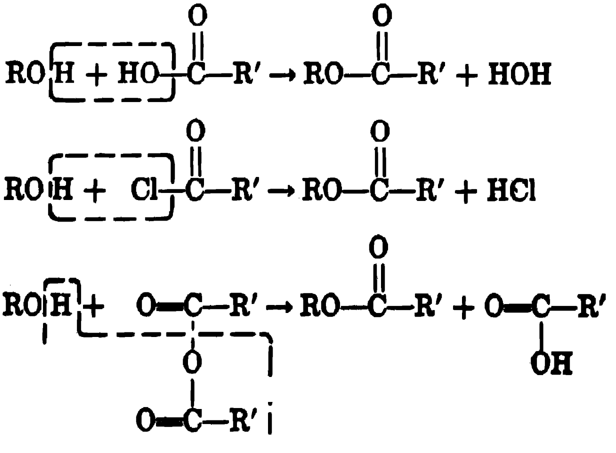
$$\overset{R\ \ H}{:\ddot{O}:} + H:\ddot{Cl}: \rightleftharpoons \overset{R\ +\ H}{\underset{H}{:\ddot{O}:}} \quad :\ddot{Cl}:^{-}$$

For example, when HBr is passed into ethyl alcohol at low temperatures, the crystalline salt $C_2H_5OH : HBr$, m.p. = −28°, precipitates out. These salts are stable only at low temperatures, and since alcohols are poor ionizing solvents, the salts exist in solution as ion pairs. When water is added to a mixture of alcohol and acid, water draws a proton away from the ROH_2^+ ion, *revealing that water is a stronger base than is an alcohol.*

This last statement may be confusing because it was stated above that water is a stronger acid than are alcohols. Several factors are involved to make water a stronger acid as well as a stronger base than are alcohols, such as solvation, electronegativities, ionic radii, and resonance. It is beyond the scope of the present treatment to discuss the contribution of all of these factors.

b. Formation of ethers. Replacement of the hydroxylic hydrogen of an alcohol by an alkyl group yields an ether. The equilibrium is unfavorable for the direct replacement through the simple reaction $ROH + RX \rightleftharpoons ROR + HX$. The cation of a metal alkoxide can readily be replaced, however; the reaction was discovered by Williamson more than a hundred years ago. The *Williamson reaction* is $RONa + R'X \rightarrow ROR' + NaX$. This is simply a displacement reaction upon R′X, and is the method of preparing unsymmetrical ethers (see Section 11.2).

c. Ester formation. An acyl group is designated by the line formula R—CO—, where R has the usual connotation. One of three reagents is commonly used as a source of acyl groups: a carboxylic acid, RCOOH, an acid chloride, R—COCl, or an acid anhydride, RCO—O—COR. Each of these three types of compounds reacts with an alcohol to replace the hydroxylic hydrogen atom by an acyl group.



$$RO\boxed{H + HO}-\overset{O}{\overset{\|}{C}}-R' \rightarrow RO-\overset{O}{\overset{\|}{C}}-R' + HOH$$

$$RO\boxed{H + \ Cl}-\overset{O}{\overset{\|}{C}}-R' \rightarrow RO-\overset{O}{\overset{\|}{C}}-R' + HCl$$

$$RO\boxed{H} + O{=}\underset{\substack{|\\O\\|\\O{=}C-R'}}{C}-R' \rightarrow RO-\overset{O}{\overset{\|}{C}}-R' + O{=}\underset{\substack{|\\OH}}{C}-R'$$

Most reactions of the hydroxylic hydrogen of alcohols also occur with phenols. Thus, the hydrogen atom may be replaced by metals, alkyl groups, or acyl groups.

$$\phi\text{—OH} + \text{Na} \rightarrow \phi\text{—ONa} + \tfrac{1}{2}\text{H}_2$$

$$\phi\text{—ONa} + \text{R—X} \rightarrow \phi\text{—OR} + \text{NaX}$$

$$\phi\text{—OH} + \text{Ac}_2\text{O} \rightarrow \phi\text{—OAc} + \text{AcOH}$$

The greater acidity of phenols also permits the replacement of the hydroxyl hydrogen by metals through reaction with alkali hydroxides.

$$\phi\text{—OH} + \text{NaOH} \rightarrow \phi\text{—ONa} + \text{H}_2\text{O}$$

The weaker an acid is the more its salt will hydrolyze; thus the order of degree of hydrolysis of the salts of carboxylic acids, phenols, and alcohols is alkoxide > phenoxide > carboxylate.

Phenols react with aqueous or alcoholic ferric chloride to give colored solutions which may be some shade of red, green, blue, or violet. This coloration is used as a diagnostic test for phenols (or enols). A colored complex ion is produced with the ferric ion. The qualitative chemical test for alcohols, as described in the section on functional group analysis (Section 21.1), is the formation of a red color with ceric ammonium nitrate solution. Phenols, however, interfere with the test.

It can be seen that the phenols and alcohols have some properties in common and some which differ. Some broad comparisons are listed in Table 10.8.

TABLE 10.8. COMPARISON OF PROPERTIES OF PHENOLS AND ALCOHOLS

$R_3C\text{—OH}$	$\phi\text{—OH}$
1. Mild pleasant odors	1. Distinct persistent odor
2. Harmless to skin	2. Severely burn the skin
3. Neutral to litmus	3. Weak acids
4. No coloration with $FeCl_{3_{aq.}}$	4. Coloration with $FeCl_{3_{aq.}}$
5. React slowly with bromine	5. React rapidly with bromine

For reactions in which the entire hydroxyl group of an alcohol is replaced, the decreasing order of reactivity is tertiary, secondary, primary. One such reaction is the replacement of OH by X.

$$3\text{ROH} + \text{PX}_3 \rightarrow 3\text{RX} + \text{P(OH)}_3$$

$$\text{ROH} + \text{PX}_5 \rightarrow \text{RX} + \text{POX}_3 + \text{HX}$$

$$\text{ROH} + \text{SOX}_2 \rightarrow \text{RX} + \text{SO}_2 + \text{HX}$$

$$\text{ROH} + \text{HX} \xrightarrow{\text{ZnCl}_2} \text{RX} + \text{HOH}$$

These reactions were given in Section 9.2 in connection with the preparation of alkyl halides from alcohols. The last reaction provides a basis for distinguishing primary, secondary, and tertiary alcohols. A solution of zinc chloride in concentrated hydrochloric acid, called *Lucas reagent*, is mixed with a few milligrams of a sample and gently warmed to 30°. In general, tertiary alcohols will react within 30 seconds, secondary alcohols will take from half a minute to five minutes, and primary alcohols will not react at this temperature. Reaction is detected by the appearance of a turbidity. Alcohols are weakly basic, and the small quantity used will normally dissolve in the strongly acidic solution owing to oxonium ion formation, but the alkyl halide product is not basic, and therefore does not dissolve. There is formed an emulsion which appears as a turbidity.

The three classes of alcohols are also distinguishable by their n.m.r. spectra. In a suitable solvent such as dimethylsulfoxide, coupling of the hydroxyl proton with H atoms on alpha carbons produces a triplet peak for a primary alcohol, a doublet for a secondary alcohol, and a singlet for a tertiary alcohol.

When mineral acids are esterified with alcohols, the tertiary alcohols exhibit the greatest reactivity, which supports the view that the OH group is being replaced:

$$R\boxed{OH + H}ONO_2 \rightarrow RONO_2 + HOH$$

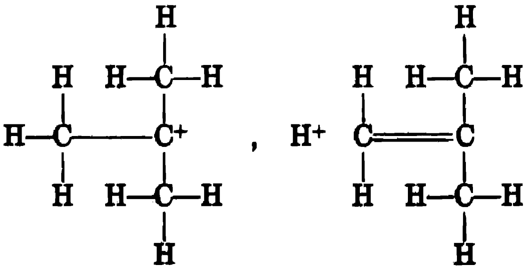
$$R\boxed{OH + H}OSO_3H \rightarrow ROSO_3H + HOH$$

It was stated above that the ease of removal of the OH group from an alcohol follows the sequence T > S > P. This can be attributed to the relative stability of the incipient carbonium ions, which decreases in this order:

$$\xrightarrow[\text{Decreasing stability}]{R_3C^+ > R_2CH^+ > RCH_2^+ > {}^+CH_3}$$

Two factors are responsible for this sequence, *hyperconjugation* and *induction* (page 343). A hydrogen atom is more electronegative than an alkyl group and therefore pulls a shared electron-pair from the positively charged carbon more than an alkyl group does. This tends to increase the positive charge on the carbon and destabilize the species. The more hydrogen atoms attached to the carbon, the greater is this destabilization, consequently, CH_3 is the least stable of the carbonium ions.

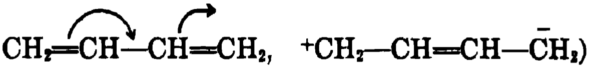
Hyperconjugation in the carbonium ions has a stabilizing effect:



(a) (b)

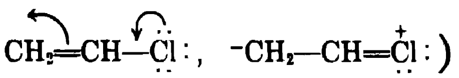
(Nine equivalent forms)

That is, this ion may be regarded as a resonance hybrid of 10 structures, and this delocalization of charge makes the ion more stable than expected on a basis of the single structure (a). Since this hyperconjugation cannot occur for the $^+CH_3$ ion, and will increase with the greater number of α C—H bonds, then the order of stability of the carbonium ions decreases in the order T, S, P. Hyperconjugation is merely resonance, but to indicate that a sigma bond is involved rather than a pi bond (as in the resonance,



$$CH_2{=}CH{-}CH{=}CH_2, \quad {}^+CH_2{-}CH{=}CH{-}\bar{C}H_2)$$

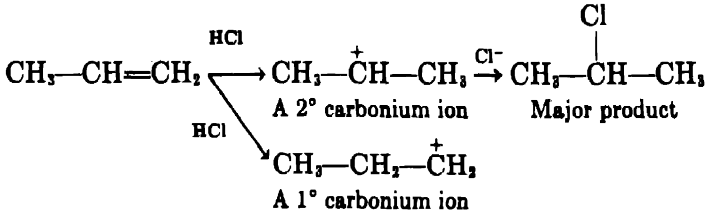
or lone-pair electrons (as in



$$CH_2{=}CH{-}\ddot{\underset{..}{Cl}}:, \quad {}^-CH_2{-}CH{=}\overset{+}{\underset{..}{Cl}}:)$$

the electron shift is called *hyperconjugation.*

Thus, we have an explanation for Markownikoff's rule concerning the direction of addition of polar molecules to an alkene. In the addition of HCl, for example, the proton attracts the π electron pair to form the more stable intermediate carbonium ion

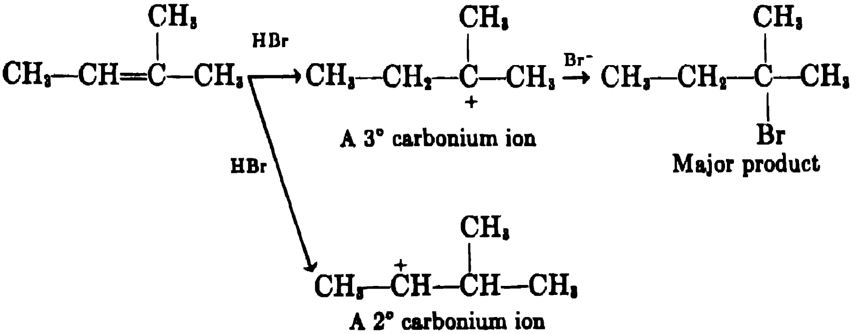


$$CH_3{-}CH{=}CH_2 \xrightarrow{HCl} CH_3{-}\overset{+}{C}H{-}CH_3 \xrightarrow{Cl^-} CH_3{-}\underset{}{\overset{Cl}{\overset{|}{C}}}H{-}CH_3$$

A 2° carbonium ion — Major product

$$CH_3{-}CH{=}CH_2 \xrightarrow{HCl} CH_3{-}CH_2{-}\overset{+}{C}H_2$$

A 1° carbonium ion



$$CH_3{-}CH{=}\overset{CH_3}{\overset{|}{C}}{-}CH_3 \xrightarrow{HBr} CH_3{-}CH_2{-}\underset{+}{\overset{CH_3}{\overset{|}{C}}}{-}CH_3 \xrightarrow{Br^-} CH_3{-}CH_2{-}\underset{\underset{Br}{|}}{\overset{CH_3}{\overset{|}{C}}}{-}CH_3$$

A 3° carbonium ion — Major product

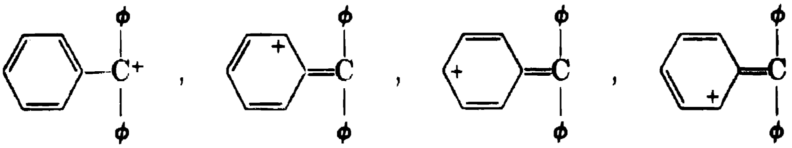
$$CH_3{-}CH{=}\overset{CH_3}{\overset{|}{C}}{-}CH_3 \xrightarrow{HBr} CH_3{-}\overset{+}{C}H{-}\overset{CH_3}{\overset{|}{C}}H{-}CH_3$$

A 2° carbonium ion

The magnitude of resonance energy is larger than hyperconjugation energy. For illustration, when there are aryl groups attached to a carbinol carbon in place of alkyl groups, the corresponding carbonium ion is stabilized to the extent that it exists in a measurable amount. For example, triphenylcarbinols behave as weak bases in concentrated sulfuric acid to yield carbonium ions.

$$\phi_3C—OH + 2H_2SO_4 \rightleftharpoons \phi_3C^+ + H_3O^+ + 2HSO_4^-$$

The presence of the carbonium ions is readily detected because they are colored. Quantitative determinations of the amount of ionization can be made from conductivity or spectroscopic measurements. The ions are much more stable than aliphatic carbonium ions because of resonance stabilization.



The ion is a resonance hybrid of many structures because the positive charge may be placed at any of the *ortho* or *para* positions of the three benzene rings. The carbonium ions are further stabilized when there are substituents in the rings which readily accept the positive charge, and such ions form one of the types of stable dyes used commercially (Section 27.3). Although the aliphatic carbonium ions are stabilized by hyperconjugation, the effect is not large enough to lead to their existence in any observable concentration. They are

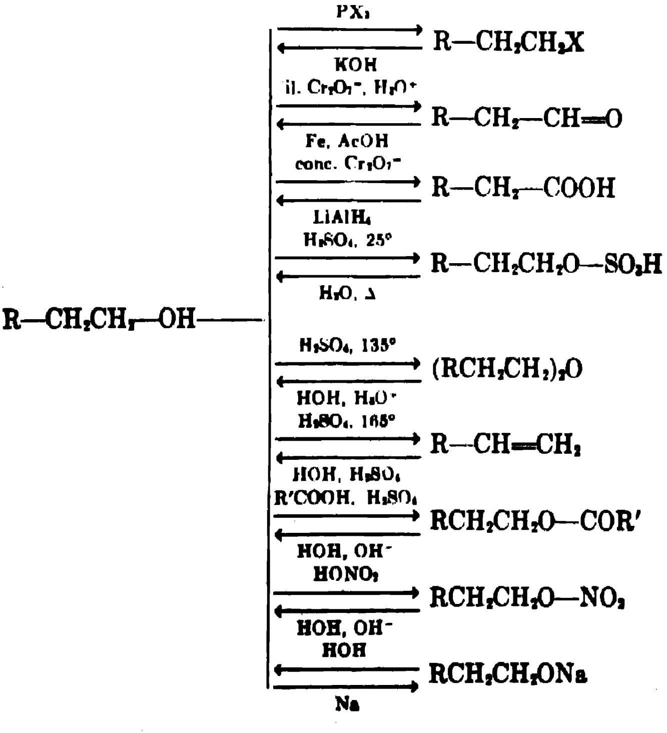


Fig. 10.2. Characteristic reaction chart for alcohols.

merely reaction intermediates and quickly undergo a change to a reaction product.

In contrast to alcohols, it is very hard to replace the OH group of a phenol. It can be reduced with zinc dust, but the reaction gives very poor yields and is impractical. Certain phosphate esters of phenols can be reduced with sodium metal in liquid ammonia in good yields.

d. Dehydration.

$$R{-}CH_2{-}CH_2OH + HOSO_3H \rightarrow R{-}CH{=}CH_2 + H_2O \cdot H_2SO_4.$$

The dehydration of alcohols was discussed in Section 3.2a as a method for preparing alkenes.

e. Oxidation. When alcohols are oxidized, various products may result, depending upon the oxidizing agent and the degree of the alcohol, i.e., primary, secondary, or tertiary.

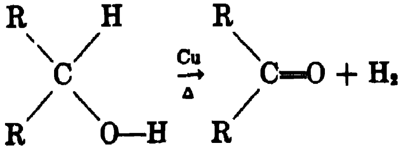
$$\underset{\substack{\text{Primary}\\ \text{alcohol}}}{R{-}CH_2OH} \xrightarrow[\text{dil. } Cr_2O_7^-]{H_3O^+} \underset{\text{Aldehyde}}{R{-}CHO} \xrightarrow[\text{conc. } Cr_2O_7^-]{H_3O^+} \underset{\text{Acid}}{R{-}COOH} \xrightarrow[\substack{\text{conc.}\\ MnO_4^-}]{} \substack{\text{degradation}\\ \text{products}}$$

$$\underset{\substack{\text{Secondary}\\ \text{alcohol}}}{R_2CHOH} \xrightarrow[\text{dil. } Cr_2O_7^-]{H_3O^+} \underset{\text{Ketone}}{R_2C{=}O} \xrightarrow{H_3O^+,\ \text{conc. } Cr_2O_7^-} \text{degradation products}$$

$$\underset{\substack{\text{Tertiary}\\ \text{alcohol}}}{R_3COH} \xrightarrow{\text{conc. } Cr_2O_7^-,\ H_3O^+} \text{degradation products}$$

The degradation products are unspecific compounds containing fewer carbon atoms than the initial reactants. For example, oxidation of *t*-butyl alcohol yields chiefly acetic acid, CH_3COOH, acetone, CH_3COCH_3, and carbon dioxide, each of which contains a smaller number of carbon atoms than the original alcohol. Observe that a primary alcohol is the only alcohol, and an aldehyde is the only carbonyl compound which will yield carboxylic acids without a loss of carbon atoms. These differences in behavior of the three classes of alcohols upon oxidation sometimes provide valuable clues in the investigation of the unknown structure of a substance.

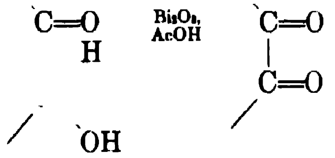
The oxidation of alcohols to carbonyl compounds is effectively a dehydrogenation, and indeed the process may be carried out by heating alcohols with copper metal.



More will be said about the selective oxidation of alcohol groups to the respective carbonyl groups in Section 12.2, where the preparation of carbonyl compounds by this method is discussed.

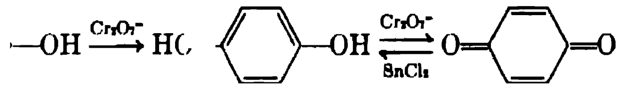
The difference in ease of oxidation of primary, secondary, and tertiary alcohols is another basis on which the three classes may be qualitatively distinguished. A drop or crystal sample of an alcohol is dissolved in 3 ml of glacial acetic acid, and a saturated, filtered, aqueous solution of potassium permanganate is added drop by drop with vigorous shaking. A tertiary alcohol will not undergo oxidation, i.e., will not change the color of the permanganate solution. If decolorization does take place, the addition of permanganate is continued until the pink color persists, then a drop of concentrated sulfuric acid is added, and more permanganate solution added dropwise. If decolorization continues, the alcohol is secondary; if the pink color is not discharged, the alcohol is primary.

Acyloins, R—CHOH—CO—R, can be selectively oxidized to diketones in good yields with Bi_2O_3 in refluxing acetic acid.



A black precipitate of bismuth metal is quickly formed. The reaction is specific for α-keto-alcohols, and even glucose gives a negative test.[3]

Oxidation of phenols. The phenol nucleus is easily oxidized, and even upon standing, phenol slowly turns brown owing to oxidation to colored products.



Phenol (white) Hydroquinone (white) *p*-Quinone (yellow)

The first step is essentially irreversible, but the hydroquinone-quinone couple is reversible. Phenol and hydroquinone have a "benzenoid" structure, i.e., the typical benzene ring, but the quinone has lost the Kekulé structure. Such a structure is referred to as a *quinoidal ring*. Quinone is a typical unsaturated ketone and undergoes addition reactions to the C=C bond and to the C=O bond. Quinone reversibly forms a molecular addition compound with hydroquinone, which is black.

$$\text{Hydroquinone} + \text{quinone} \rightleftharpoons \text{quinhydrone}$$

The bonding between the hydroquinone and quinone portions of quinhydrone cannot be represented in the usual fashion, so a structural formula will not be given here (see Section 19.1). The two molecules are present in a 1:1 ratio in the addition product.

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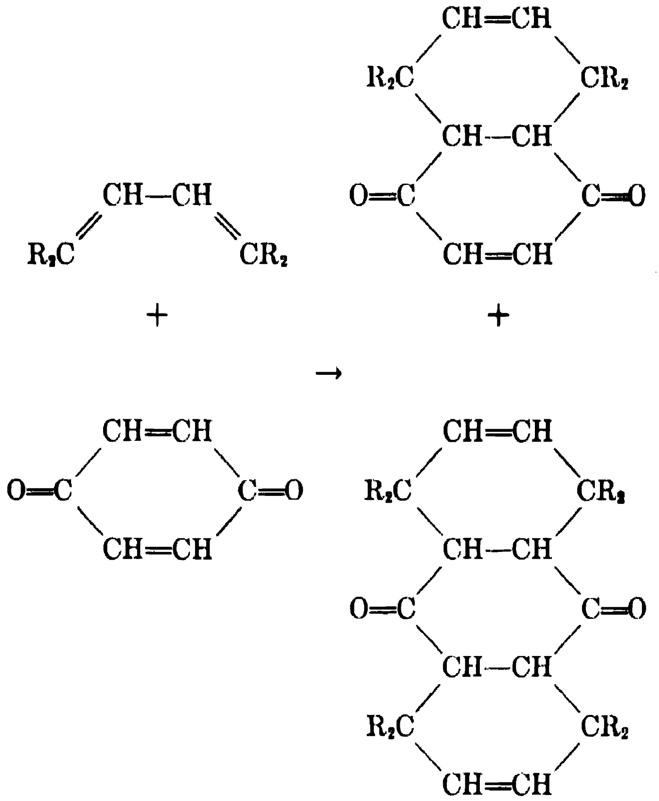
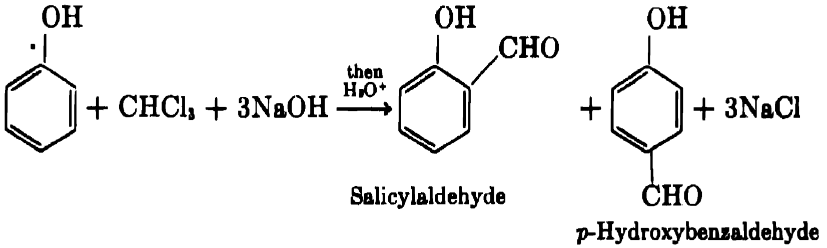
[3] W. Rigby, *J. Chem. Soc.*, 793 (1951).

Quinone is sometimes used in place of maleic anhydride in the Diels-Alder reaction. It will add to one or two moles of a conjugated diene.

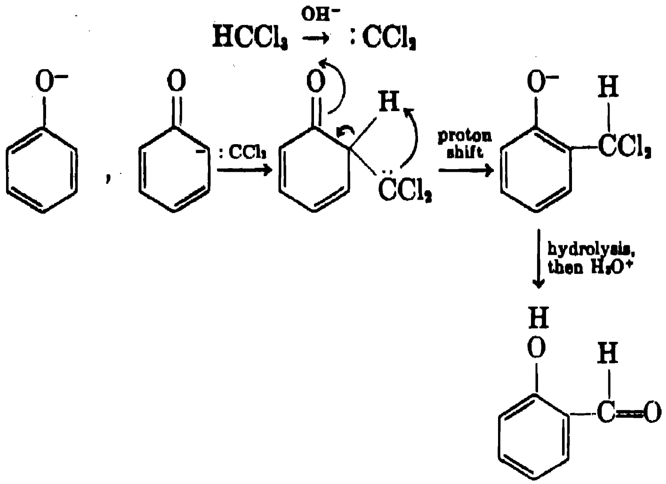


f. Nuclear reactions of phenols. The OH group is one of the strongest ring-activating groups and leads to several reactions which take place only with phenols.

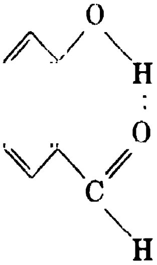
Reimer-Tiemann reaction:



The chloroform reacts with the base to form dichlorocarbene, and the phenoxide ion is a resonance hybrid with a large electron-density at the ortho and para carbons:

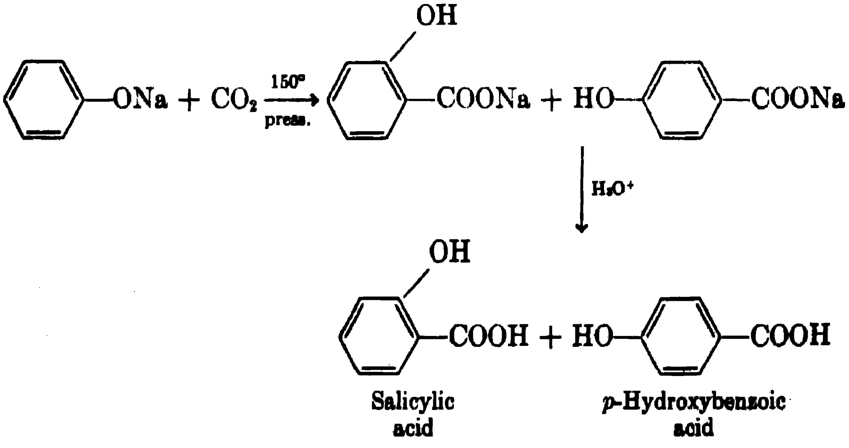


Yields are very small with *m*-orienting groups in the ring. The isomeric products are easily separated by steam distillation. As a result of association through hydrogen bonds, the *p*-hydroxybenzaldehyde is soluble in hot water; it is therefore not steam distillable. In the *ortho* isomer, the OH group forms an intramolecular hydrogen bond with the CHO group.



This prevents association with water and also increases volatility. As a result, the *ortho* isomer is steam distillable.

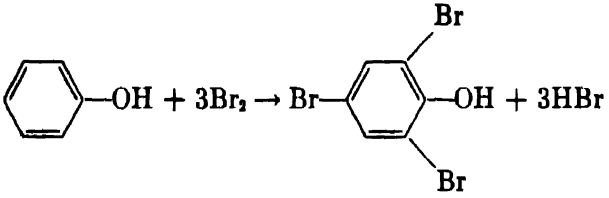
Kolbe-Schmitt reaction:



Again, two isomers are obtained, but in this case they must be separated by fractional crystallization. The *ortho* isomer has a common name, whereas the *m*- and *p*-hydroxybenzoic acids are named as such. It is interesting that in the Kolbe-Schmitt reaction the alkali salts give different ratios of the *ortho* and *para* hydroxy acids.

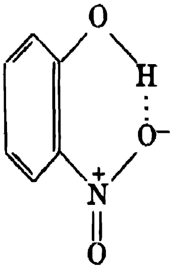
Lithium salt gives 100% *ortho*, 0% *para*
Sodium salt gives 75% *ortho*, 25% *para*
Potassium salt gives 25% *ortho*, 75% *para*

The strong ring-activating effect of OH causes phenols to be halogenated very rapidly. At room temperature, phenol gives tribromophenol almost as rapidly as the reagents are mixed.



At temperatures below 5°, monobromination can be achieved, producing primarily the *para* isomer.

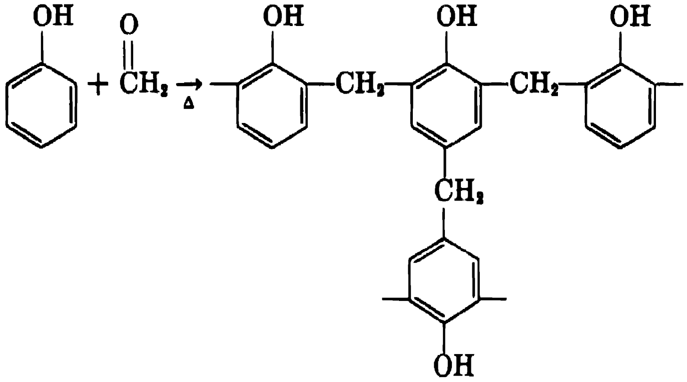
Phenol can be mononitrated or monosulfonated at low temperatures. Nitration of phenol with dilute nitric acid yields a mixture of *o*- and *p*-nitrophenol, which can be resolved by steam distillation. The OH group of the *para* isomer associates with water to make the phenol quite soluble in hot water, but the OH group of the *ortho* isomer is tied up by an intramolecular hydrogen bond.



This bonding prevents association with water, thereby decreasing its water solubility, and also gives it a higher vapor pressure. Consequently, the *ortho* isomer is steam distillable, while the *para* isomer is not. *o*-Nitrophenol also has lower melting and boiling points than the *meta* and *para* isomers. Cf Table 10.5.

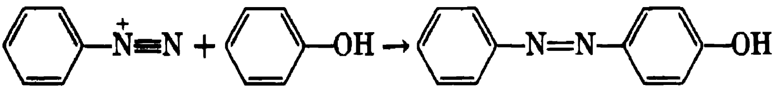
Phenols give colors with aqueous ferric chloride which may be red, green, blue, or violet. This coloration is used as a characteristic color test for phenols (in the absence of enols). A colored complex ion is produced with the ferric ion.

Phenols condense with aldehydes to form polymers. The most widely known example is Bakelite, discovered by Leo Baekeland in 1907:



Polycondensation takes place in two dimensions to give a tough, nonelastic polymer.

Phenols condense with diazonium salts to yield deeply colored azo products (cf. pages 410 and 598).

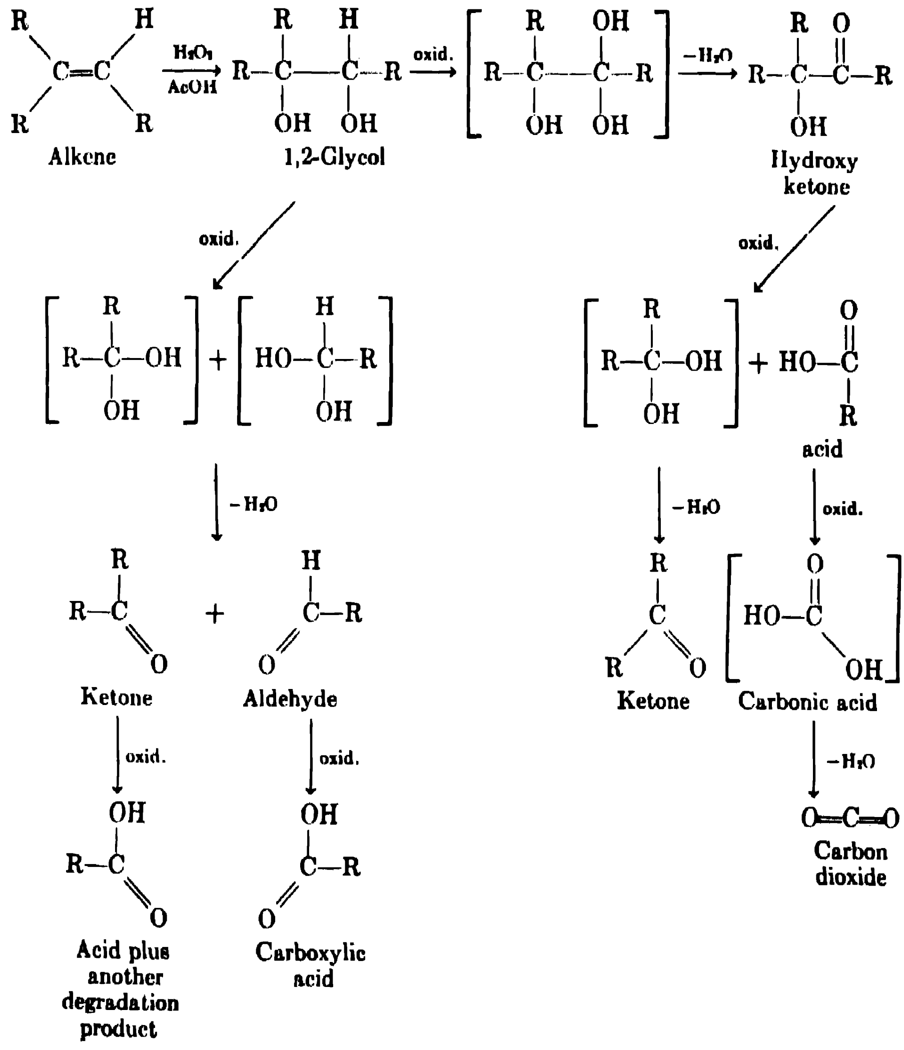


p-Hydroxyazobenzene

10.7 OXIDATIONS OF ORGANIC COMPOUNDS

When carbon atoms suffer oxidation, usually a C—C or a C—H bond is broken and an OH becomes attached to the oxidized carbon atom. For instance, it was shown in Section 3.4 that the first oxidation product of an alkene is a 1,2-glycol. Further oxidation of the glycol results in cleavage of a C—H or C—C bond to the oxygenated carbon atoms, and the course of oxidation may follow several alternative routes, depending upon the oxidizing agent. For illustration, various possible oxidation products from an alkene are shown on page 279. Note that aldehydes, ketones, carboxylic acids, or CO_2 may be formed, depending upon the oxidizing agent used, the experimental conditions, and the structure of the original alkene. Usually the C—C bond of the glycol is not broken until all the hydroxylic C—H bonds have been oxidized, and C—H bonds of saturated carbons suffer no oxidation.

Observe that in all the bracketed structures shown, there are two OH groups on one carbon atom. Such compounds are rarely stable enough to



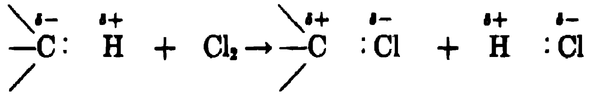
allow their isolation; they lose HOH to yield a C=O bond. This is the case for the familiar carbonic acid, H_2CO_3, which has never been isolated. In water solution it is in equilibrium with CO_2.

Another aspect of oxidation-reduction reactions is the matter of stoichiometry. Seldom is it necessary to balance the equation for a redox reaction completely, but merely to determine the reacting molar ratio between oxidant and reductant. This involves an arbitrary assignment of oxidation levels to elements in organic compounds, which will be shown presently.

When a sodium atom loses an electron to become a sodium ion, it has undergone an oxidation, and when a chlorine atom gains an electron to become a chloride ion, it has undergone a reduction. That is, oxidation is regarded as the loss of electrons, and reduction as the gain of electrons. With organic compounds, the complete gain or loss of electrons is not as apparent. Covalent bonds consist of electron pairs being shared by two atoms, with the distribution between the two atoms depending upon their relative electronegativities. For example, from Table 10.9 the relative electronegativities of carbon and hydrogen are such that the electron pair of a C—H bond lies somewhat nearer the carbon atom than the hydrogen atom. On the other hand, in a C—Cl bond, the greater electronegativity of chlorine draws the electron pair closer to the chlorine atom. Therefore, in a chlorination reaction

TABLE 10.9. RELATIVE ELECTRONEGATIVITY VALUES OF SOME ELEMENTS

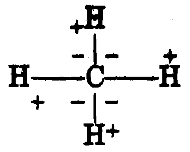
			H = 2.1			
Li 0.97	Be 1.47	B 2.01	C 2.50	N 3.07	O 3.50	F 4.10
Na 1.01	Mg 1.23	Al 1.47	Si 1.74	P 2.06	S 2.44	Cl 2.83
						Br 2.74
						I 2.21

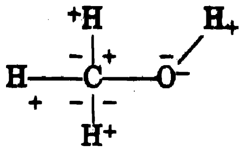


$$-\overset{\delta-}{\mathrm{C}}:\ \overset{\delta+}{\mathrm{H}} + \mathrm{Cl_2} \rightarrow -\overset{\delta+}{\mathrm{C}}\ \ :\overset{\delta-}{\mathrm{Cl}} + \overset{\delta+}{\mathrm{H}}\ \ :\overset{\delta-}{\mathrm{Cl}}$$

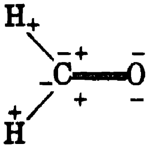
an electron pair is drawn away from carbon, not completely, but only partially. Nevertheless, this limited withdrawal of electrons may be regarded as a partial oxidation, since oxidation is the loss of electrons.

In this sense covalent atoms may be considered to undergo oxidation or reduction. The oxidation stage of an atom, then, is dependent upon the type of atoms with which it forms bonds. For a given atom, bonds with more electronegative atoms raise its level of oxidation, and bonds with less electronegative atoms decrease its stage of oxidation (i.e., raise its level of reduction), whereas bonds between like elements do not affect the stage of oxidation. For example, the oxidation stage of carbon in CH_4 and CH_3OH may be considered to be −4 and −2, respectively.

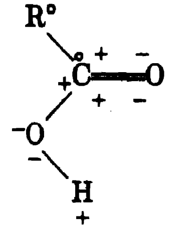




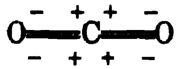
Other examples for carbon are as follows (O.S. = oxidation stage):



O.S. = 0



O.S. = +3



O.S. = +4

In this fashion, the relative oxidation stages of all elements in any organic compound may be determined;[4] however, seldom is it necessary. The major concern in an oxidation-reduction reaction is to know the stoichiometric relationships between the oxidizing agent and the reducing agent, so that the proper quantities may be used when carrying out the particular reaction. Fortunately, this information may be determined without the oxidation stage of atoms in organic molecules being known. In other words, one wishes merely to be able to write a balanced equation for a given redox reaction. There are several methods for doing this, and it is quite arbitrary which method one chooses. The method recommended here[5] is quite simple and is applicable to all ordinary reactions. It will be presented here with one illustration given. A detailed explanation is given in Section A7 of the Appendix.

There are two general approaches commonly used for balancing equations for oxidation-reduction reactions: the valence change method and the half-reaction method. The former is usually the quicker for simple cases, but sometimes reactions are encountered which are baffling to balance by this method. Furthermore, it is more difficult to ascertain oxidation numbers for carbon in organic substances. Hence the half-reaction method is used here because the procedure is very simple and straightforward and will handle any example to be encountered. If desired, a valence-change procedure is given in the Appendix, and although it will usually be quicker in its application, it is more difficult to teach.

Procedure: The recommended procedure involves three or four steps for balancing each half-reaction, depending on whether it is for an acidic or alkaline medium.

---

[4] L. N. Ferguson, "Balancing Equations for Organic Oxidation-Reduction Reactions," *J. Chem. Educ.* **23**, 550 (1946).

[5] The author is indebted to Dr. Gus Dorough, formerly of Washington University, St. Louis, for suggesting this method.

Step 1: Balance all elements except hydrogen and oxygen.

Step 2: Bring oxygen to a balance with H_2O molecules, then bring hydrogen to a balance with protons.

Step 3: Balance ionic charges with electrons.

Step 4 (for alkaline media): Remove excess protons by adding an equal number of hydroxide ions to both sides of the arrow.

Illustration: Write a balanced equation for the oxidation of

$$CH_3{-}CH{=}C(NH_2){-}CHOH{-}CH_2CH_3$$

to $CH_3COOH + HOOC{-}CO{-}CH_2CH_3 + N_2$ with $K_2Cr_2O_7$ in acid solution.

Solution:

Step 1: The C's appear to be balanced by merely writing down the reactants and products. In order to balance nitrogen, one merely writes down $\frac{1}{2}$ mole of N_2 being formed.

$$CH_3{-}CH{=}C(NH_2){-}CHOH{-}CH_2CH_3 \rightarrow CH_3COOH + HO_2C{-}CO{-}C_2H_5 + \tfrac{1}{2}N_2 \quad (1)$$

Step 2: When counting oxygen atoms, it is found that there is 1 on the left and 5 on the right side, so 4 H_2O's are added to the left.

$$4H_2O + CH_3{-}CH{=}C(NH_2){-}CHOH{-}CH_2CH_3 \rightarrow CH_3COOH + HO_2C{-}CO{-}C_2H_5 + \tfrac{1}{2}N_2.$$

Now there are 21 H's on the left and 10 on the right, so add 11 H^+ to the right side.

$$4H_2O + CH_3CH{=}C(NH_2){-}CHOH{-}CH_2CH_3 \rightarrow CH_3CO_2H + HO_2C{-}CO{-}C_2H_5 + \tfrac{1}{2}N_2 + 11H^+ \quad (2)$$

Step 3: In (2) there are no ionic charges on the left, and there are 11 positive ionic charges on the right; therefore charges are brought to a balance by adding 11 electrons to the right. This gives a balanced half-reaction.

$$4H_2O + CH_3CH{=}C(NH_2){-}CHOH{-}CH_2CH_3 \rightarrow CH_3CO_2H + HO_2C{-}CO{-}CH_2CH_3 + \tfrac{1}{2}N_2 + 11H^+ + 11e^- \quad (3)$$

For the dichromate half-reaction:

Step 1: $Cr_2O_7^{=} \rightarrow 2Cr^{+3}$

Step 2: Add 7 H_2O's to right side to balance oxygen.

$$Cr_2O_7^{=} \rightarrow 2Cr^{+3} + 7H_2O$$

Add 14 H^+'s to left side to balance hydrogen.

$$14H^+ + Cr_2O_7^{=} \rightarrow 2Cr^{+3} + 7H_2O \quad (4)$$

Step 3: With $+14 - 2 = +12$ ionic charges on the left and $2(+3) = +6$ on the right, charges are brought to a balance by adding 6 electrons (i.e., 6 negative charges) to the left side. The balanced half-reaction then becomes:

$$6e^- + 14H^+ + Cr_2O_7^{=} \rightarrow 2Cr^{+3} + 7H_2O \tag{5}$$

Now, in order to combine the two half-reactions, an equal number of electrons in each is obtained by finding the lowest common denominator (LCD) and multiplying each by the quotient. Here, LCD $= 6 \times 11 = 66$; hence, $66/11 = 6$ times equation (3), and $66/6 = 11$ times equation (5). The two are then combined and common items canceled.

6 × (3)

$$24H_2O + 6CH_3CH{=}C(NH_2){-}CHOH{-}CH_2CH_3 \rightarrow$$
$$6CH_3COOH + 6HO_2C{-}CO{-}CH_2CH_3 + 3N_2 + 66H^+ + 66e^-$$

11 × (5)

$$66e^- + 154H^+ + 11Cr_2O_7^{=} \rightarrow 22Cr^{+3} + 77H_2O$$

$$\begin{aligned} &6CH_3CH{=}C(NH_2){-}CHOH{-}CH_2CH_3 \rightarrow 6HO_2C{-}CO{-}CH_2CH_3 \\ &+ 24H_2O + 66e^- + 154H^+ + 11Cr_2O_7^{=} \quad + 6CH_3COOH + 3N_2 + 66H^+ \\ &\qquad + 66e^- + 22Cr^{+3} + 77H_2O \end{aligned}$$

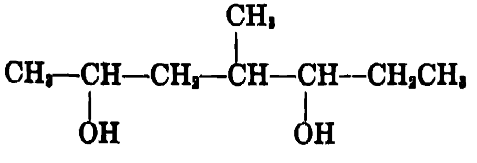
Subtracting $24H_2O$, $66e^-$, and $66H^+$ from both sides leaves

$$\begin{aligned} &6CH_3CH{=}C(NH_2){-}CHOH{-}CH_2CH_3 \rightarrow 6HO_2C{-}CO{-}CH_2CH_3 \\ &+ 88H^+ + 11Cr_2O_7^{=} \qquad + 6CH_3COOH + 3N_2 \\ &\qquad + 22Cr^{+3} + 53H_2O \end{aligned} \tag{6}$$

This is the balanced equation sought, and a check of charges and matter reveals that they balance. For more detailed explanations of the procedure, see Section A7 of the Appendix.

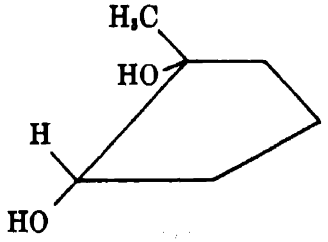
10.8 POLYHYDRIC ALCOHOLS

Dihydric alcohols are called *glycols* (Gr. *glykeros*, sweet, *ol*, alcohol) but their generic name according to the Geneva system has the suffix *diol* with numerical prefixes to indicate the positions of the OH groups. Examples are the following:



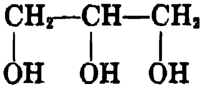
$$CH_3{-}\underset{OH}{\underset{|}{CH}}{-}CH_2{-}\overset{CH_3}{\overset{|}{CH}}{-}\underset{OH}{\underset{|}{CH}}{-}CH_2CH_3$$

4-Methyl-2,5-heptanediol



1-eMthyl-*cis*-1,2-cyclopentanediol

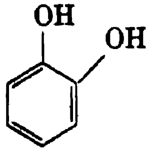
Compounds containing three OH groups are called *triols*, and the one of largest value is 1,2,3-propanetriol, known to every chemist as *glycerol* and as *glycerine* at the corner drugstore.



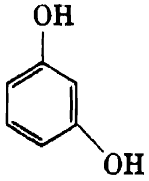
$$\underset{\displaystyle OH}{CH_2}—\underset{\displaystyle OH}{CH}—\underset{\displaystyle OH}{CH_2}$$

Glycerol

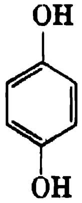
Several polyhydric phenols are quite common, and most of them have trivial names.



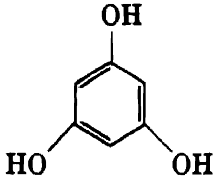
Catechol



Resorcinol



Hydroquinone

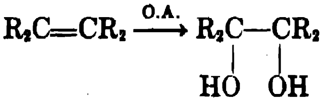


Phloroglucinol

They exhibit the same properties as phenol in general but are much more reactive.

a. Preparation of 1,2-glycols. The 1,2-glycols, commonly called *pinacols*, are probably the most important of the glycols, and several general methods of preparation are used.

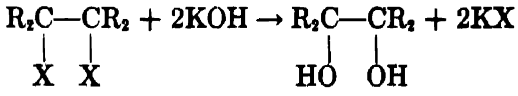
Oxidation of olefins (page 103):



$$R_2C{=}CR_2 \xrightarrow{O.A.} \underset{\displaystyle HO}{R_2C}—\underset{\displaystyle OH}{CR_2}$$

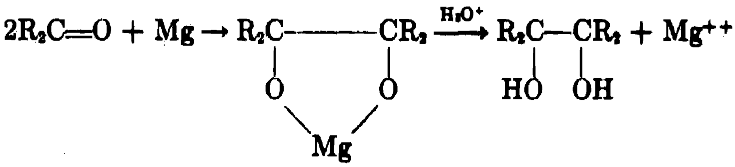
O.A. = MnO_4^-, Na_2CO_3 aq.
or
H_2O_2, AcOH

Hydrolysis of vic. dihalides:



$$\underset{\displaystyle X}{R_2C}—\underset{\displaystyle X}{CR_2} + 2KOH \rightarrow \underset{\displaystyle HO}{R_2C}—\underset{\displaystyle OH}{CR_2} + 2KX$$

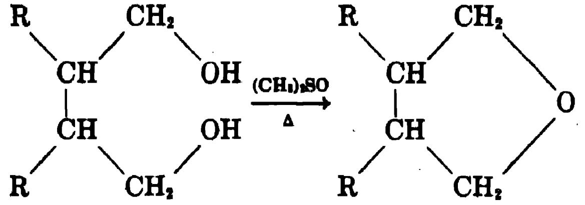
Pinacol reduction of ketones:



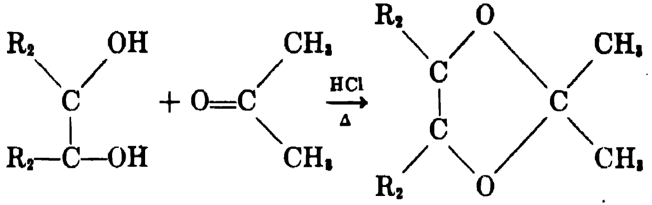
$$2R_2C{=}O + Mg \rightarrow \underset{\displaystyle O\searrow_{Mg}\swarrow O}{R_2C——CR_2} \xrightarrow{H_3O^+} \underset{\displaystyle HO}{R_2C}—\underset{\displaystyle OH}{CR_2} + Mg^{++}$$

Other types of glycols may be made by the methods employed to make monohydric alcohols, starting with the appropriate compounds.

b. Properties of glycols. Glycols have the same general chemical and physical properties discussed previously for the monohydric alcohols, but owing to the presence of two hydroxyl groups, they have additional properties. One is the formation of cyclic compounds. For instance, cyclic products are formed intramolecularly or with carbonyl compounds:

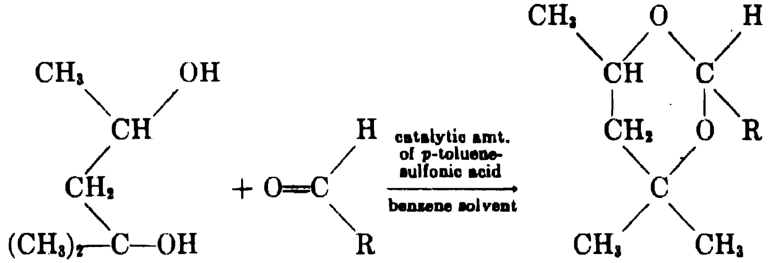


1,4-Diols Tetrahydrofurans



1,2-Diols Acetonides

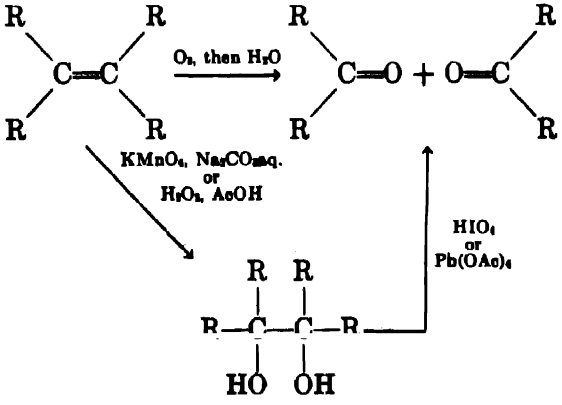
This reaction is sometimes used for the formation of derivatives of 1,2-glycols in their identification.



2-Methyl-2,4-pentanediol A 1,3-dioxane

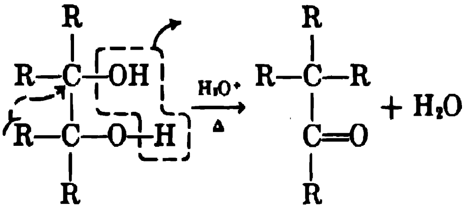
The pentanediol appears to form the 1,3-dioxane ring only with aldehydes and therefore has been used to separate aldehydes from ketones.

The 1,2-glycols can be cleaved to the corresponding carbonyl compounds by oxidation with lead tetraacetate or periodic acid. Thus, there are two routes from an olefin to the two respective carbonyl compounds.

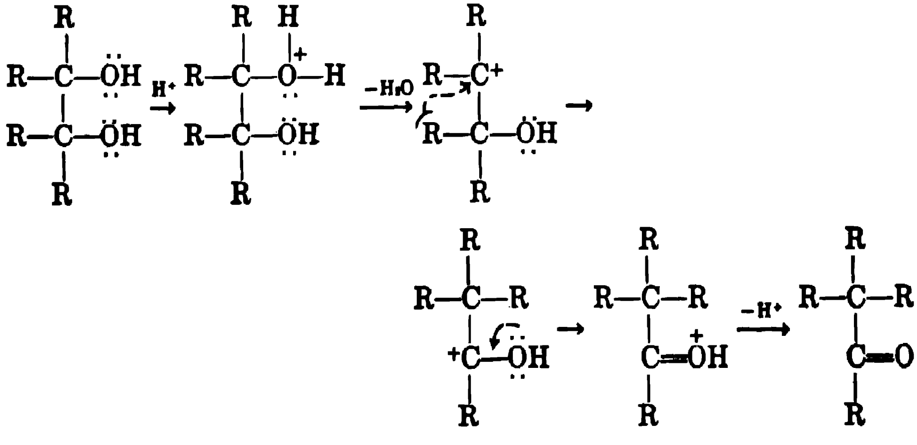


The periodic acid reagent provides a basis for the qualitative detection of 1,2-glycols. When periodic acid oxidizes a 1,2-glycol, the periodate ion is reduced to iodate ion. If silver nitrate is added, silver iodate will precipitate. Silver periodate is quite soluble, so that the appearance of the white precipitate indicates the presence of iodate ion brought about by the reduction of periodate ion by a 1,2-glycol.

Pinacol rearrangement: When heated in dilute mineral acid, pinacols, i.e., 1,2-glycols, undergo a molecular rearrangement to pinacolones.

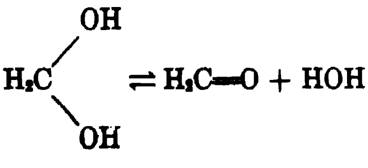


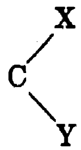
The reaction consists in a loss of a molecule of water from the two OH groups and a migration of an alkyl group to the adjacent carbon atom.

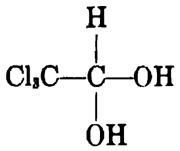


Such molecular rearrangements in organic chemistry are not uncommon and differ from tautomerism in that the reactions are not readily reversible. Other types of rearrangements will be encountered throughout this book.

c. Special glycols. The simplest glycol, $H_2C(OH)_2$, is unstable and cannot be isolated. It exists in aqueous solution where it is in equilibrium with formaldehyde and water.



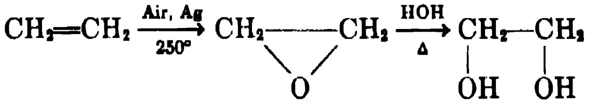
This is consistent with the observation that compounds of the type  $C\begin{smallmatrix}\diagup X\\ \diagdown Y\end{smallmatrix}$ are usually too unstable to be isolated, where X may be OH or NH_2, and Y may be OH, OR, NH_2, NR_2, OCOR, SH, or a halogen atom. If Y is a strongly electronegative group, such as COOH, SO_3H, or CN, the compounds may be isolated but are easily decomposed. Increasing the electronegativity of the carbon atom also increases the stability of such compounds. Thus, with the strongly electronegative group CCl_3 attached to carbon, the corresponding 1,1-glycol is stable and isolable.



$$Cl_3C-\overset{\displaystyle H}{\underset{\displaystyle OH}{\overset{|}{\underset{|}{C}}}}-OH$$

Trichloroacetaldehyde hydrate or chloral hydrate

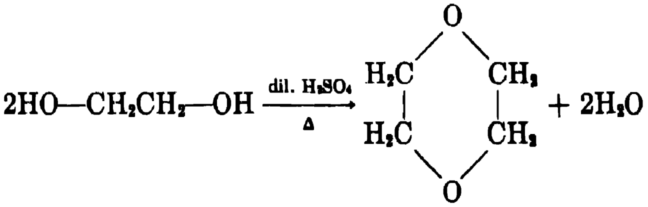
The next higher glycol, ethylene glycol, is the most common of the family. Most of it is prepared commercially by the air oxidation of ethylene to ethylene oxide, which is then hydrolyzed to the glycol:



Ethylene oxide

Ethylene glycol

When ethylene glycol is heated with dilute aqueous sulfuric acid, *1,4-dioxane* is produced:



Dioxane is a valuable solvent because it dissolves many organic substances and is also completely miscible with water. When ethylene glycol is heated with a dehydrating agent like phosphoric acid, water is lost between two OH groups and *polyethylene glycols* are obtained:

$$HOCH_2CH_2OH + HOCH_2CH_2OH \xrightarrow{H_3PO_4}$$

$$HOCH_2CH_2-O-CH_2CH_2OH + H_2O$$

Diethylene glycol

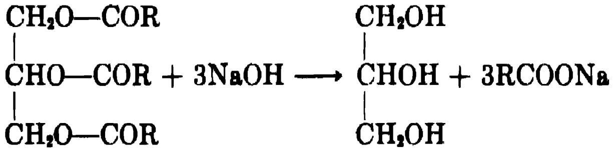
$$n\ \mathrm{HOCH_2CH_2OH} \xrightarrow{\mathrm{H_3PO_4}}$$

$$\mathrm{HOCH_2CH_2{-}O{-}(CH_2CH_2O)_{n-2}{-}CH_2CH_2OH} + (n-1)\ \mathrm{H_2O}$$

These polyethylene glycols contain alcohol (OH) and ether (C—O—C) functional groups. This makes them soluble in water and they range from viscous liquids to waxlike solids (Carbowaxes).

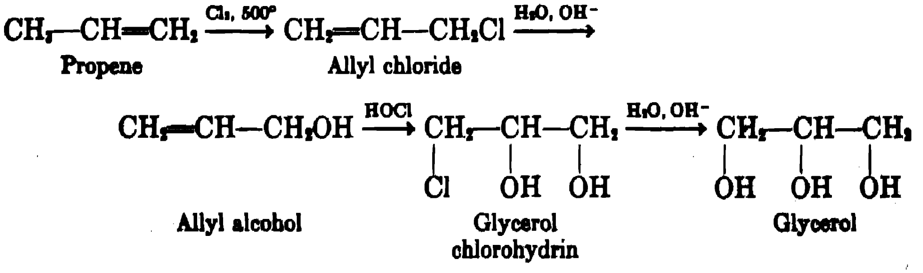
d. Glycerol. In the laboratory, glycerol could be prepared by any of the reactions used for preparing monohydric alcohols, but the commercial production of glycerol is chiefly by one of two methods. The older of the two methods is by the hydrolysis of fats:

Fat + alkali gives glycerol + soap



$$\begin{array}{l} \mathrm{CH_2O{-}COR} \\ | \\ \mathrm{CHO{-}COR} \\ | \\ \mathrm{CH_2O{-}COR} \end{array} + \mathrm{3NaOH} \longrightarrow \begin{array}{l} \mathrm{CH_2OH} \\ | \\ \mathrm{CHOH} \\ | \\ \mathrm{CH_2OH} \end{array} + \mathrm{3RCOONa}$$

A *fat* is a triester of glycerol, and its hydrolysis yields glycerol plus the metal-ion salt of a carboxylic acid, called a *soap*. In colonial days this reaction was performed for the purpose of making soap, by using meat tallow as a source of fat and ashes to provide the alkali. During World War II the housewife's grease drippings were taken to the butcher in exchange for meat coupons, because the fat was needed to produce glycerol and soap for the war effort. The soap was used in the production of synthetic rubber as an emulsifying agent, and the glycerol was used, among other things, in the production of smokeless-powder explosives and plastics. However, there was a demand for much more glycerol than could be obtained from available fats, and industry sought other sources. The method finally adopted was a synthesis from propene:

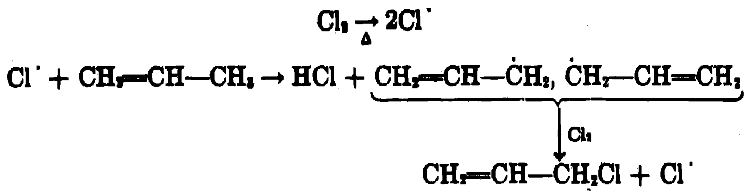


$$\underset{\text{Propene}}{\mathrm{CH_3{-}CH{=}CH_2}} \xrightarrow{\mathrm{Cl_2,\ 500^\circ}} \underset{\text{Allyl chloride}}{\mathrm{CH_2{=}CH{-}CH_2Cl}} \xrightarrow{\mathrm{H_2O,\ OH^-}}$$

$$\underset{\text{Allyl alcohol}}{\mathrm{CH_2{=}CH{-}CH_2OH}} \xrightarrow{\mathrm{HOCl}} \underset{\text{Glycerol chlorohydrin}}{\begin{array}{ccc} \mathrm{CH_2} & \mathrm{-CH-} & \mathrm{CH_2} \\ | & | & | \\ \mathrm{Cl} & \mathrm{OH} & \mathrm{OH} \end{array}} \xrightarrow{\mathrm{H_2O,\ OH^-}} \underset{\text{Glycerol}}{\begin{array}{ccc} \mathrm{CH_2} & \mathrm{-CH-} & \mathrm{CH_2} \\ | & | & | \\ \mathrm{OH} & \mathrm{OH} & \mathrm{OH} \end{array}}$$

This has been a highly successful procedure and accounts for a major portion of the present-day production of glycerol.

In the chlorination of propene at 500°, substitution takes place instead of addition, owing to the high reactivity of chlorine atoms.



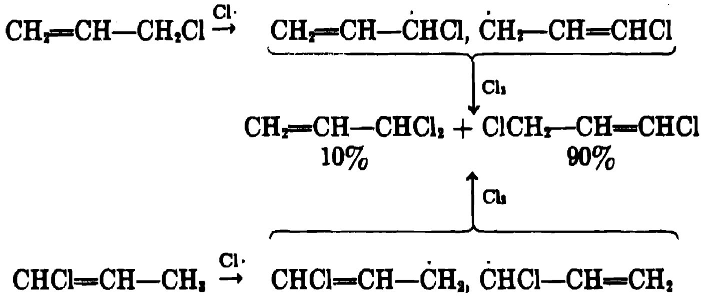
$$Cl_2 \xrightarrow[\Delta]{} 2Cl^{\cdot}$$

$$Cl^{\cdot} + CH_2{=}CH{-}CH_3 \rightarrow HCl + \underbrace{CH_2{=}CH{-}\dot{C}H_2,\ \dot{C}H_2{-}CH{=}CH_2}$$

$$\Big\downarrow Cl_2$$

$$CH_2{=}CH{-}CH_2Cl + Cl^{\cdot}$$

The allyl radical is a resonance hybrid of two equivalent structures, and although it is not discernible, the chlorine atom in allyl chloride is attached to the former CH_2 group in some molecules and to the former CH_2 group in other molecules. If the C's are labeled with isotopic carbon or with substituents, then the resonant hybrid nature of allyl radicals is apparent. For example, the same proportion of dichlorination products is obtained when starting with $CH_2{=}CH{-}CH_2Cl$ as with $CHCl{=}CH{-}CH_3$:



$$CH_2{=}CH{-}CH_2Cl \xrightarrow{Cl\cdot} \underbrace{CH_2{=}CH{-}\dot{C}HCl,\ \dot{C}H_2{-}CH{=}CHCl}$$

$$\Big\downarrow Cl_2$$

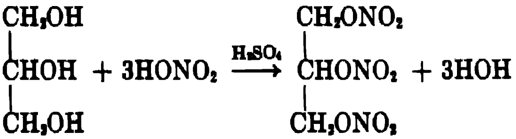
$$\underset{10\%}{CH_2{=}CH{-}CHCl_2} + \underset{90\%}{ClCH_2{-}CH{=}CHCl}$$

$$\Big\uparrow Cl_2$$

$$CHCl{=}CH{-}CH_3 \xrightarrow{Cl\cdot} \overbrace{CHCl{=}CH{-}\dot{C}H_2,\ \dot{C}HCl{-}CH{=}CH_2}$$

Evidence against the notion that the mechanism of chlorination of propene involves the addition of Cl_2 followed by elimination of HCl is the fact that pyrolysis of 1,2-dichloropropane does not give the same product as high-temperature chlorination of propene.

Glycerol can be esterified with mineral acids just as the monohydric alcohols are. The trinitrate ester, commonly called *trinitroglycerine* may be obtained with nitric acid.



$$\begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array} + 3HONO_2 \xrightarrow{H_2SO_4} \begin{array}{l} CH_2ONO_2 \\ | \\ CHONO_2 \\ | \\ CH_2ONO_2 \end{array} + 3HOH$$

10.9 USES OF HYDROXY COMPOUNDS

Among the organic chemicals produced commercially, ethanol and methanol rank second and third in quantity of annual production. Methanol is used largely (1) as a solvent in the plastics and textile industries, (2) for rinsing metal and glass parts in various industries, (3) for power boosters in gasoline engines, (4) for antifreezes, and (5) for the production of formaldehyde (see Section 12.2). Commercial airliners burn a carburetor injection mixture of 60 per cent methanol and 40 per cent water, which increases power on take-off. It is fed to the engines for about 40 seconds, automatically cutting off after the plane is air-borne. Carburetor injection mixtures based on methanol are also used in racing cars and motorboats.

Ethyl alcohol is used extensively in a large number of manufacturing operations: (1) as a starting material for synthetic products, (2) as a processing solvent, and (3) as an ingredient of commercial products. Lacquers, varnishes, medicinal extracts, flavoring extracts, perfumes and cosmetics, organic chemicals, photographic materials, dyes, inks, synthetic rubber, radiator antifreezes, and fuel are some of the commodities for which alcohol is employed in their manufacture.

Isopropanol is an effective germicide. It is used as a rubbing compound for massage purposes, in lotions, liniments, liquid soaps, and antiseptic solutions.

The toxicity of hydroxylic compounds fluctuates considerably from compound to compound. For instance, methyl alcohol is very toxic; small amounts taken internally may produce blindness or may even be fatal. Ethyl alcohol is fairly nontoxic, although it produces definite physiological effects (page 256). Ethylene glycol is quite toxic. It is oxidized to oxalic acid by the body, whereupon calcium oxalate deposits in the renal tubes, causing anuria. Diethylene glycol, $(HOCH_2CH_2)_2O$, is very toxic. In 1937 over 70 people died as a result of medication with a solution of sulfanilamide in diethylene glycol. On the other hand, propylene glycol, $CH_3—CHOH—CH_2OH$, is nontoxic. Allyl alcohol is very toxic, and even contact with the skin is to be avoided.

Ethylene glycol is commonly used in "permanent" antifreezes. Its second largest use is in the manufacture of ethylene glycol dinitrate for low-freezing dynamite. Glycerol trinitrate is a powerful explosive which formerly was soaked up by sawdust for stabilization and sold as dynamite. Today, dynamites have other ingredients besides nitroglycerine, particularly, ethylene glycol dinitrate. At one time most accidents involving dynamite resulted from its freezing. By lowering the freezing point of dynamite, ethylene glycol dinitrate has helped to make it safer to handle. Ethylene glycol is also used as a moistening agent for cellophane and in the manufacture of plastics and antiseptics.

In addition to being used in the production of explosives and plastics,

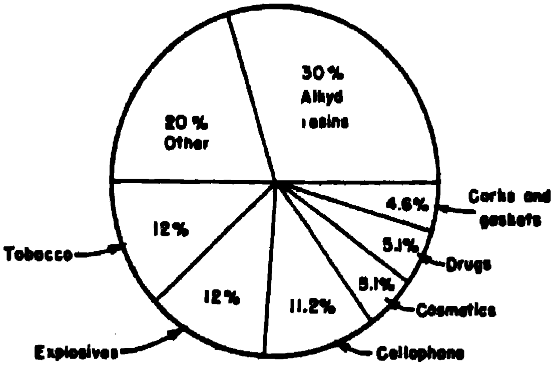


Fig. 10.3. Glycerol use pattern.

glycerol is used as a moistening agent for tobacco, as a softening agent for cellophane films, in cosmetics, in food products, and as a commercial solvent. The glycerol use-pattern is shown in the chart in Figure 10.3.

A large fraction of our phenol supply goes into the production of plastics (Bakelite) and resins. Phenols are also used in preparing dyes, photographic developers, wood preservatives, flavoring agents, local anesthetics, drugs, and perfumes.

STUDY EXERCISES

1. Give three general equations for preparing primary and secondary alcohols and two for preparing tertiary alcohols.
2. How are the following compounds prepared commercially: (a) methyl alcohol, (b) commercial ethyl alcohol, (c) absolute ethyl alcohol, (d) 1-propanol, (e) isopropyl alcohol, (f) glycerol, (g) ethylene glycol, (h) phenol?
3. How is alcohol produced from carbohydrates?
4. What is meant by the term "associated liquid"?
5. How does intermolecular hydrogen bonding affect two properties of hydroxylic compounds?
6. What is the order of reactivity of 1-butanol, 2-butanol, and *t*-butyl alcohol toward (a) sodium metal, (b) PCl_5, (c) esterification by an organic acid, (d) esterification by nitric acid, (e) dehydration by sulfuric acid?
7. What is meant by the terms "soap" and "fat"?
8. What reagents would be used to convert ethyl alcohol into (a) chloroethane, (b) acetaldehyde, (c) acetic acid, (d) ethyl ether, (e) ethylene, (f) ethyl acetate, (g) ethyl nitrate, (h) ethyl nitrite, (i) sodium ethoxide, (j) ethyl hydrogen sulfate?
9. What are the structures of the first stable oxidation products of *n*-propyl and isopropyl alcohols?
10. Using graphic formulas, write equations for the production of *t*-butyl and isobutyl alcohols from isobutylene.
11. Write the structural formulas for (a) 1-hexene-3-yne-5-ol; and (b) 2-nitro-1,3-propanediol.
12. Write structural formulas for the 8 pentyl alcohols. Name each isomer and write the formula for the first oxidation product of each primary and secondary alcohol.
13. If one knew the boiling points of ethyl and propyl alcohols, how could he estimate the boiling point of 1-pentanol? Carry out this procedure and check the estimate with the known value.
14. A liquid of boiling point 197°C. is completely miscible with water. Can it be a monohydric alcohol?
15. How are phenols prepared in the laboratory?
16. Using structural formulas, diagram the addition of quinone to isoprene.
17. How do phenols and aliphatic alcohols compare in acidity, toxicity to the skin, color with aqueous ferric chloride, and reactivity to bromine?
18. Illustrate by equations the reaction of *m*-cresol (*m*-methylphenol) with (a) sodium metal, (b) sodium hydroxide, (c) bromine at room temperature, (d) alkali plus chloroform.
19. Explain the fact that triphenylcarbinol yields a measurable amount of carbonium ion in sulfuric acid but that tricyclohexylcarbinol does not.
20. How could each of the following be prepared using a Grignard reagent and the

appropriate carbonyl compound: (a) *n*-pentyl alcohol, (b) 2-pentanol, (c) 3-methyl-3-pentanol, (d) 1-phenyl-1-butanol, (e) 3-pentene-2-ol, (f) 1-methylcyclopentanol?

21. Offer an explanation for the trend in heats of hydrogenation of the following alkenes:

$CH_2{=}CH_2$	32.0 kcal/mole
$CH_3{-}CH{=}CH_2$	30.1
trans-2-butene	27.6
2-Methyl-2-butene	26.9
Tetramethylethylene	26.6

22. *cis*-1,2-Cyclopentanediol reacts with acetone plus dry HCl to give a compound M, $C_8H_{14}O_2$. M is inert to hot aq. NaOH but readily produces 1,2-cyclopentanediol in aqueous acid. Propose a structure for M and explain the fact that *trans*-1,2-cyclopentanediol does not give a compound such as M.

TEST QUESTIONS, Set 10

1. How could a solid alcohol be distinguished from a solid paraffin?

2. What series of reactions could you use to transform *n*-propyl alcohol into (a) isopropyl iodide, (b) *n*-hexane, (c) propyne, (d) *n*-butyl alcohol?

3. If ethyl alcohol is used to produce ethylene, how many liters of ethylene, measured at 25° and 730 mm, could be obtained from 10 moles of alcohol, if the yield in the reaction is 80 per cent? What volume, measured at the same temperature and pressure, if the yield is 90 per cent and 10 liters of alcohol is used which is 92 per cent pure (sp. gr. = 0.813)?

4. Why can one predict that oxidation of 2-hydroxybutane would give $CH_3{-}CO{-}CH_2{-}CH_3$ and not 2,3-dihydroxybutane?

5. Can calcium chloride be used to dry the lower alcohols? Why, or why not? If it cannot be used, what drying agents may be used?

6. If 1-g samples of methyl and ethyl alcohols are separately treated with an excess of methylmagnesium iodide, what volume of methane will be evolved at STP in each case?

7. The molecular weight of water in the liquid state is a multiple of 18. Give a possible explanation.

8. How can one determine the quantity of alcohol in a mixture of (a) alcohol and *n*-hexane, (b) alcohol and *n*-hexene?

9. How can one distinguish by qualitative test-tube experiments (a) ethanol from ethyl ether, (b) sodium propoxide from sodium hydroxide, (c) 1,3-pentanediol from 1,2-pentanediol, (d) isobutyl alcohol from isopropyl alcohol, (e) allyl alcohol from *n*-propyl alcohol?

10. When treated with potassium metal, 1.84 g of a monohydric alcohol gave off 448 ml of hydrogen, STP. What is the molecular weight of the alcohol? What would be the molecular weight if it were a dihydric alcohol?

11. Write a balanced equation for the oxidation of 1-butene to CH_3CH_2COOH plus CO_2 with potassium dichromate in acid solution.

12. What weight of potassium dichromate would be required to oxidize 1 mole of $CH_3{-}CHOH{-}CH_2{-}CHO$ to $CH_3{-}CO{-}CH_2{-}COOH$ in acid solution?

13. Ten grams of a mixture of hexane and ethanol are reacted with excess sodium metal, and 224 ml of hydrogen STP are collected. What is the percentage of alcohol in the mixture?

14. One mole of a substance reacts with acetyl chloride and it is found that 2 moles

of acetyl chloride are consumed. The product has the molecular formula $C_9H_{16}O_4$. What is the molecular weight of the original substance?

15. What weight of potassium dichromate would be required to oxidize 29 g of $CH_3—CH═CH—CHOH—CHOH—CH_3$ which is 80 per cent pure to $CH_3CHO + HOOC—COOH + CH_3CHO$ in acid solution if the dichromate salt is only 92 per cent pure?

16. Write a balanced equation for the oxidation of $CH_3CH_2C(NH_2)═CH—CHOH—CO—COOH$ to $CH_3CH_2COOH + N_2 + 4CO_2$ with potassium permanganate in acid and in alkaline solutions.

17. A compound S when treated with ozone gives compound T. When T is treated with water it gives the same two compounds as does the oxidation of $CH_3—CH(CH_3)—CHOH—CHOH—CH_2CH_3$ with periodic acid. What are the structures of S, T, and the two oxidation products?

18. What quantities of organic substances would be required to make 17.6 g of 3-pentanol from CH_3CH_2CHO and any desired chemicals?

19. A compound X, $C_7H_{14}O$, has an infrared band in dilute CCl_4 at 3628 cm^{-1}, none in the 1680–1725 cm^{-1} range, and is inert to cold aq. $KMnO_4$. Upon oxidation with hot aq. potassium dichromate in sulfuric acid, a compound $C_7H_{12}O_4$ is recovered which neutralizes two equivalents of sodium hydroxide. Propose two possible structures for X and give the basis for your answer.

20. What relative weights of methyl alcohol, ethyl alcohol, and ethylene glycol are required to produce the same lowering of the freezing point of water when added to a given volume of water?

21. On what basis would one expect methane and water to have nearly the same boiling points? What are the actual facts and how do you explain them?

22. What would be the chief products formed in the dehydration with sulfuric acid of (a) 2-hexanol, (b) 2-methyl-3-hexanol, (c) 4-methyl-3-hexanol, (d) 3-methyl-2-hexanol?

23. If one were to distill 98 per cent ethyl alcohol very carefully through a fractionating column for the purpose of getting pure alcohol, would he want the distillate? Why, or why not?

24. Explain the fact that diethyl sulfide, $(C_2H_5)_2S$, boils at a higher temperature than ethanethiol, C_2H_5SH, but ethyl alcohol has a much higher boiling point than ethyl ether, $(C_2H_5)_2O$.

25. On the basis of the respective boiling points, propose a stereo structure for 1,3-cyclohexanediol: 1,3-cyclohexanediol, *boiling point* 65°
1,4-cyclohexanediol, *boiling point* 100–102°
cis-1,2-cyclohexanediol, *boiling point* 104

26. How could one demonstrate that hexa-*p*-tolylethane $[(p\text{-}CH_3C_6H_4)_3C—C—(C_6H_4—CH_3\text{-}p)_3]$ dissociates in benzene solution?

27. How could you distinguish 3,4,5-trimethylphenol from triphenylcarbinol by qualitative test-tube experiments?

28. Which solution will have the larger *p*H, 1 *M* sodium phenoxide or 1 *M* sodium acetate?

29. How could one distinguish by qualitative test-tube experiments (a) cyclohexanol from phenol, (b) *p*-cresol (*p*-methylphenol) from benzoic acid, (c) picric acid from phenol, (d) 2,4,6-trimethylphenol from 3,5-dimethylphenol?

30. What weight of sodium dichromate would be required to oxidize 1 mole of hydroquinone to quinone?

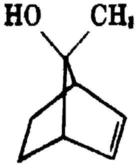
31. 2,6-Dimethylphenol dissolves in alkali and gives a color with aqueous ferric chlo-

ride, but 2,6-di-*t*-butylphenol does not. Can you think of a possible explanation for this unusual behavior of the latter compound?

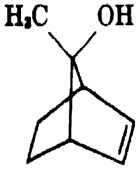
32. Predict the order of increasing solubility in water for chloroform, bromoform, and carbon tetrachloride. Explain the basis for your prediction and compare it with the observed facts. (Solubilities in g/100 g H_2O at 20°: $CHCl_3$, 0.82; $CHBr_3$, 0.1; CCl_4, 0.08.)

33. Account for the observation that the infrared carbonyl frequency in salicylaldehyde (*o*-HO—C_6H_4—CHO) is lower (1666 cm^{-1}) than that of *m*-hydroxybenzaldehyde (1700 cm^{-1}).

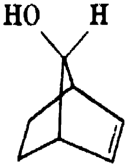
34. On the basis of the infrared data given below, what structure would you assign compound I (ν_{OH} = 3622 cm^{-1}), Ia or Ib?



Ia

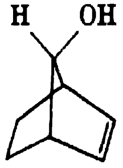


Ib



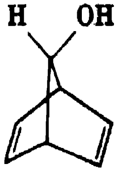
II

ν_{OH} = 3628 cm^{-1}



III

ν_{OH} = 3572 cm^{-1}

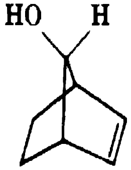


IV

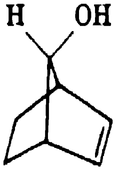
ν_{OH} = 3551 cm^{-1}

Give the basis for your reply. If compound I were hydrogenated to the saturated bicyclo alcohol, what frequency would you predict for its ν_{OH}?

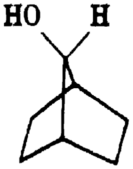
35. Three unlabeled bottles are known to contain a different one of the following compounds:



R



S



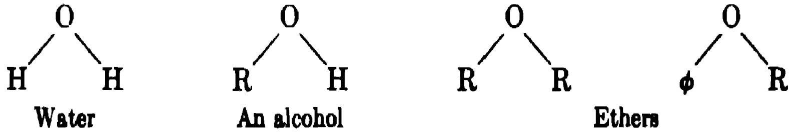
T

What spectral measurements would you make to identify the contents of each bottle?

11

Ethers

Ethers comprise the class of compounds in which two carbon-attached groups are joined to a single oxygen atom, or what may be regarded as a disubstitution product of water.



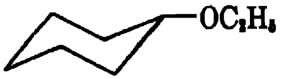
Water An alcohol Ethers

The attached groups of the ether may or may not be alike. Ethers in which the groups are not alike are referred to as *mixed*, or *unsymmetrical*, *ethers*. The most common of all ethers, ethyl ether $C_2H_5—O—C_2H_5$, is usually just called *ether*.

11.1 NOMENCLATURE

The Geneva system suggests that ethers be named as alkoxyl derivatives of other classes of compounds. The common or trivial way of naming ethers is to name the organic groups attached to the oxygen atom and add the word ether.[1] Some examples are as follows:

$CH_3—CH_2CH_2—O—CH_2CH_2CH_3$



1-(*n*-Propoxy)-propane
or
n-propyl ether

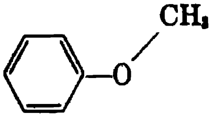
Ethoxycyclohexane
or
cyclohexyl ethyl ether

---

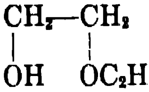
[1] The prefixes di-, tri-, etc., are used to indicate two or more simple groups, as in 3,3-dimethylpentane or trichloromethane. For two or more identical complex groups, the prefixes *bis*- and *tris*- are used. The prefix *bi*- is used to denote a double molecule formed by the union of 2 like molecules through the loss of hydrogen. For example, biphenyl is $C_6H_5—C_6H_5$, and bicyclohexyl is $C_6H_{11}—C_6H_{11}$. The I.U.C. has agreed that radicals with two identical groups attached do not need the prefix di-. Thus, $CH_3—O—CH_3$ is methyl ether, not dimethyl ether, and $(C_2H_5O)_2SO_2$ is ethyl sulfate, not diethyl sulfate. This is consistent with the practice of naming inorganic salts, for $MgCl_2$ is magnesium chloride, not magnesium bichloride, and Na_2SO_4 is sodium sulfate, not disodium sulfate.

$C_6H_5-O-C_6H_5$

Phenyl ether

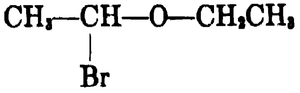


Phenyl methyl ether or anisole



$$\begin{matrix} CH_2 & - & CH_2 \\ | & & | \\ OH & & OC_2H_5 \end{matrix}$$

Ethylene glycol monoethyl ether
or
β-ethoxyethanol



$$\begin{matrix} CH_3-CH-O-CH_2CH_3 \\ | \\ Br \end{matrix}$$

1-Ethoxy-1-bromoethane
or
α-bromoethyl ethyl ether

$Cl-CH_2CH_2-O-CH_2CH_2-Cl$

1-(2-Chloroethoxy)-2-chloroethane
or
bis-(β-chloroethyl) ether

11.2 PREPARATION

a. Catalytic dehydration of alcohols.

$$2ROH \xrightarrow[250^\circ]{Al_2O_3} ROR + HOH$$

$$ROH + HOSO_3H \xrightarrow{-HOH} ROSO_3H \xrightarrow{R'OH} ROR' + H_2SO_4$$

It will be recalled from Section 3.2 that the reaction of alcohols with sulfuric acid produces an alkyl hydrogen sulfate, which yields an ether at about 135° in the presence of more alcohol. At higher temperatures the alkyl hydrogen sulfate produces an alkene.

b. Williamson synthesis. This is the most practical method of making mixed ethers.

$$RONa + R'X \rightarrow ROR' + NaX$$

The reaction gives good yields, is simple to carry out, and can be applied to the preparation of aryl ethers:

$$\phi-ONa + RX \rightarrow \phi-OR + NaX$$

The industrial preparation of ethers is, in general, through modifications of these laboratory methods. Frequently syrupy phosphoric acid is used as the catalyst in place of sulfuric acid.

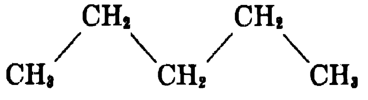
11.3 PHYSICAL PROPERTIES

Ethers are nonassociated substances and have boiling points (Table 11.1) near what would be expected on a basis of their molecular weights. Thus, their boiling points are near those of the respective hydrocarbons in which

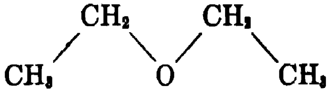
TABLE 11.1. PHYSICAL CONSTANTS OF SOME ETHERS

Name	*Melting Point*	*Boiling Point*
Methyl ether	−140	−24
Ethyl ether	−116	34.6
n-Propyl ether	−122	91
n-Butyl ether	−95	142
Isopropyl ether	−60	69
Vinyl ether		35
Allyl ether		94
Anisole	−37	154
Ethyl phenyl ether	−33	172
Phenyl ether	27	259
Ethylene oxide	−111	14
Tetrahydrofuran	−108	66
1,4-Dioxane	11	101

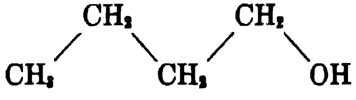
CH_2 occurs in place of the ether oxygen atom. In Table 10.2 it was shown that R—O—R and R—CH_2—R have boiling points fairly close. In Section 10.5 was discussed how the lack of association results in normal boiling points for substances whereas association with water tends to make compounds water soluble. For illustration, *n*-pentane and ethyl ether are nonassociated liquids and boil at much lower temperatures than does *n*-butanol.



n-Pentane
B.P. = 36°
insoluble in H_2O



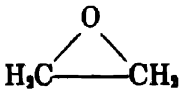
Ethyl ether
B.P. = 34.5°
8% soluble in H_2O



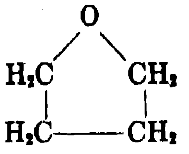
n-Butanol
B.P. = 118°
9% soluble in H_2O

The OH group of water, however, can form hydrogen bonds with the oxygen atoms of the ether and the alcohol molecules, making them more soluble in water than pentane. Thus the association of water with alcohol and ether molecules gives them greater water solubilities than hydrocarbons, and co-association of alcohol molecules with themselves gives them higher boiling points than their isomeric ether molecules.

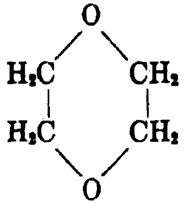
The lack of complete solubility of the first few ethers in water appears to be due to a spatial hindrance of the alkyl groups which blocks the close approach of aggregated liquid water molecules. For instance, the cyclic ethers ethylene oxide, tetrahydrofuran, and dioxane,



Ethylene oxide



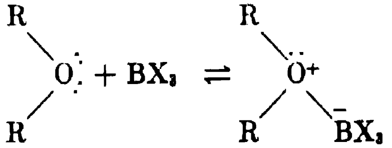
Tetrahydrofuran

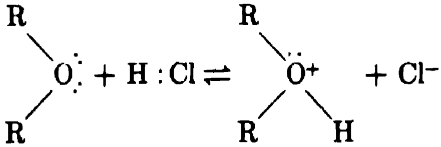


Dioxane

are each completely miscible with water, whereas the corresponding open chain ethers are not.[2]

A divalent oxygen atom has two pairs of unshared electrons, one pair of which it is willing to share with an agent (Lewis acid) that strongly wants an electron pair to complete its valence shell.[3] In other words, the oxygen atom is weakly basic, weaker even than a trivalent nitrogen atom. Accordingly, the oxygen will share an electron pair (neutralize) with only a strong acid, producing an oxonium ion or salt.





The oxonium ions are quite soluble in concentrated acid solutions, such as concentrated hydrochloric and sulfuric acids, and therefore, ethers and alcohols are moderately soluble in these acids. Again, water is a stronger base than is an ether and can liberate the ether from its salt.

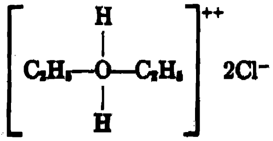
$$HOH + R_2\overset{+}{O}H \rightarrow R_2O + H_3O^+$$

A dilute solution of acid, therefore, will not form the oxonium ion to any practical extent (the protons being tied up by water molecules), and the solubilities of ethers in dilute acid solutions and in water are not significantly different.

---

[2] L. N. Ferguson, *J. Amer. Chem. Soc.* 77, 5288 (1955).

[3] Under rare circumstances, the oxygen will even share its second pair of electrons. For instance, the dihydrochloride salt of ethyl ether, m.p. = −88°, is known:

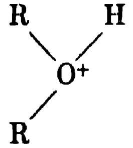


$$\left[C_2H_5-\overset{\displaystyle H}{\underset{\displaystyle H}{O}}-C_2H_5 \right]^{++} 2Cl^-$$

Because of this electron-donor character of ethers, they also dissolve certain metal salts, such as RMgX, $MgCl_2$, $FeCl_3$, etc. The cations of these salts accept and share electron pairs and are thereby brought into solution.

11.4 CHEMICAL PROPERTIES

Ethers are almost as inert as alkanes to the common laboratory reagents. For example, they are inert to alkali and cold or dilute acids and to most reducing and oxidizing agents, including aqueous permanganate. In the presence of strong acids ethers are slowly hydrolyzed. This is the result of oxonium ion formation,



in which either the O—H or an R—O bond may break. The former is the stronger, but at times favorable intermolecular collisions occur to give some molecules an extra amount of energy in which an R—O bond may break. In these cases, an R—O—H molecule is left, and the R^+ picks up an anion (OH^- or X^-) from the solution. Hence, ethers are slowly cleaved in acid media but not in basic media. The stronger the acid, the more rapid is the hydrolysis. When an HX acid is used, the alcohol molecules initially formed in the hydrolysis are converted to RX molecules, so that two alkyl halide molecules result.

$$R—O—R + 2HX \rightarrow 2RX + HOH$$

This reaction is used occasionally as a method of characterizing an ether. Its applicability depends upon the ease of separating and identifying the two RX products.

11.5 ETHER AND ANESTHESIA

Because of the absence of an effective analgesic prior to the middle of the nineteenth century, surgery was performed only when absolutely necessary, and then the fully conscious patients were usually bound with ropes or held forcibly by assistants to prevent their escaping the surgeon's knife. When the operations required freedom from struggling, the victims were sometimes drugged with alkaloids or intoxicants, sometimes hypnosis was attempted, or cruel methods were used to produce temporary loss of consciousness, such as striking a wooden bowl placed on the head, or even half-strangulation.

Joseph Priestly isolated nitrous oxide in 1766 and Sir Humphrey Davy demonstrated its analgesic effects in 1799. In 1844 an American dentist, Horace Wells, administered nitrous oxide while extracting teeth. His first anesthesia trials were successful, and he introduced the gas into general dental practice. However, one patient awakened prematurely, screaming with pain, and another case was fatal, and Wells was forced to withdraw from practice. He became embittered, depressed, and finally insane, and committed suicide at the age of 33. In this same period, a Boston chemist, Charles Jackson, etherized himself and persuaded a dentist, William Morton, to try it. Morton did and then persuaded a surgeon, John Warren, to give a public demonstration of surgery with ether anesthesia. The operation in 1846 was painlessly completed, and soon general anesthesia was widely adopted for surgical operations. Morton patented his preparation, but a great "ether controversy" arose.

A Georgia physician, Crawford Long, had used ether anesthesia in surgery and obstetrics several years prior to the Morton-Warren experiment. However, he did not publish his observations nor try to bring ether into general anesthesia until 1848, when he gave a report to the Georgia Medical Society. Long, Morton, Jackson, and the descendents of Wells made claims for the $100,000 prize offered by the U.S. Congress. The controversy continued for years and the award was never made. Embittered by the dispute, Morton died of apoplexy in 1868 and Jackson became insane.

The development of local anesthesia soon followed. Koller, a medical student in Vienna, first demonstrated the practical use of cocaine in 1884, and Hall introduced it into dentistry that same year. However, Novocain has been the standard local anesthetic for years. Today anesthesiology is a highly skilled profession and of major concern in surgery.

Important factors in anesthesia are depth of unconsciousness, speed of action, physiological side effects and after effects and ease of administration. Ethyl ether is still the most widely used anesthetic because it is easy to administer and causes excellent relaxation of the muscles. If any other agent had been used with the careless methods of earlier times, anesthetic mortality would have been tremendous. Blood pressure, pulse rate, and rate of respiration are usually only slightly affected. Ether's chief drawbacks are its irritating effect on the respiratory passages and its after effect of nausea. Nitrous oxide is pleasant to inhale and rapid in its action, and often it is used to induce unconsciousness and pave the way for more potent drugs, such as ether.

Vinyl ether does not have the nauseous after effect and is a rapid-acting, short-term anesthetic. It is favored for the doctor's home and office use, but must be used with caution to prevent too deep a level of unconsciousness. Methyl propyl ether is claimed to be less irritating and more potent than ethyl ether. Cyclopropane (C_3H_6) will produce deep anesthesia, and would be about the best anesthetic if it were not explosive and did not require so much skill in its administration. The anesthetic properties of cyclobutane are much like those of cyclopropane. Cyclopentane, however, elicits unconsciousness with clonic convulsions. Trifluoroethyl vinyl ether has been found suitable for man, but hexafluoroethyl ether induces violent convulsions upon inhalation.

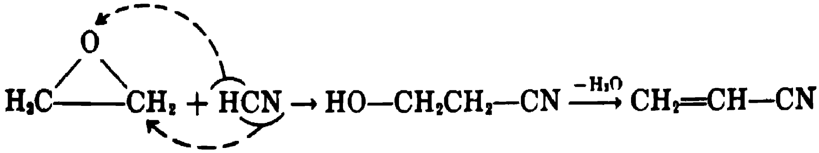
A recent widely used anesthetic is *Halothane*, $C_2HBrClF_3$. It is nonflammable, nonexplosive, and causes minimum discomfort to the patient. Although a few cases of liver damage have been attributed to its use, millions of patients have had operations under *Halothane*, and such a safety record is statistically impressive. Only a physician can serve as an anesthesiologist. Except in emergencies, he studies the patient in advance of operations to decide the best anesthetic to use. Before an operation, a patient gets a tranquilizer, usually a barbiturate. Later he may get a morphine-type drug, and next he may be given atropine to keep mucus from clogging his air passages. Finally, in the operating room he is given something to put him to sleep. Alleviation of pain is important to the surgeon as well as to the patient, and no other class of drugs has contributed more to human welfare than the anesthetics. They have changed the operating room from a place of horror to one of tranquility.

Anesthetics relieve pain by rendering the person unconscious. Narcotic analgesics (see Section 24.4) deaden pain by raising the threshold to pain and diminishing the alarm reaction to sustained pain. The latter is often accompanied by addiction and altered mental alertness. Between these two extremes are the nonnarcotic analgesics, such as aspirin, which obtund pain by increasing the threshold to pain but act at a subcortical level and thereby do not interfere with mental alacrity. The preeminence of aspirin in public health is found in the fact that Americans use it in its various dosage forms to the extent of 21 tons *daily*.

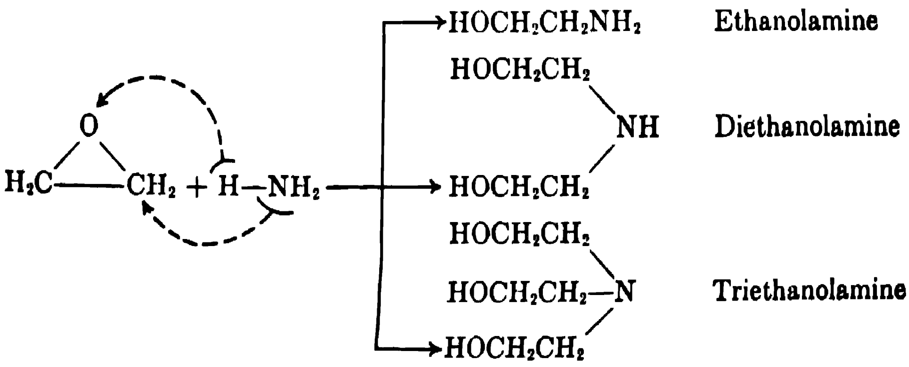
The mechanism of action of anesthetics is unknown. Correlations have been observed between anesthetic potency and certain physical properties such as oil/water distribution coefficients, water solubility, vapor pressure, adsorbability, and stability of clathrate hydrates. These generalizations have led to various theories about the mode of action of anesthetics but correlations do not prove a theory, so that no one knows yet how these agents produce the state of unconsciousness.

11.6 CYCLIC ETHERS

Certain cyclic ethers are quite common. Dioxane, made industrially by dehydrating ethyl alcohol or diethylene glycol or by dimerizing ethylene oxide, is an important solvent because it dissolves most organics and is miscible with water. It is used to prepare partially aqueous solutions of organic substances. Tetrahydrofuran is a common solvent for metal hydride reductions (see Chapter 20). Over 61 million pounds of acrylonitrile are made annually for the production of plastics and synthetic rubber. Most of the acrylonitrile is made from ethylene oxide.



Ethylene oxide is also used to make ethanolamines and nonionic detergents.



Almost a billion pounds of ethylene oxide are consumed annually in the automotive, aircraft, plastic, rubber, synthetic detergent, and textile industries.

STUDY EXERCISES

1. Give two general equations for the preparation of ethers.
2. How could an impurity of ethyl ether be removed from *n*-pentane?

3. How would one distinguish propyl ether from *n*-heptanol?

4. Write equations for the preparation of (a) ethyl cyclopentyl ether, (b) *n*-propyl ether, (c) *n*-propyl isobutyl ether, (d) anisole.

5. How would you prepare methyl cyclopropyl ether?

TEST QUESTIONS, Set 11

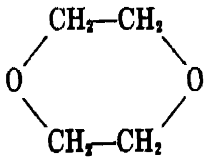
1. If ethyl ether were a linear molecule would it have a dipole moment?

2. Why has hydrogen chloride a very large solubility in ether and in water but only a moderate solubility in *n*-hexane and in carbon tetrachloride?

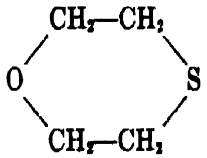
3. What *n*-alkane should boil near the boiling point of *n*-propyl ether?

4. Why do Grignard reagents dissolve in ethers but not in alkanes? Could absolute ethyl alcohol be used as a solvent for Grignard reagents?

5. Predict the relative boiling points of dioxane and 1,4-thioxane.



Dioxane



1,4-Thioxane

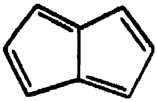
Three-Hour Examination I

The student should have an idea of how well he has grasped the material on the basis of how many of the Study Exercises and Test Questions he can answer without aid of the book. However, he may wish to test his proficiency by taking a timed examination on the material. Such a test is therefore provided here. Not all classes will reach the same point in the book at the end of the first semester, but the ethers represent a reasonable stage at which to take such an examination. The questions are of the type given in the Test Questions, but here there is a wider sampling of material than that found in the Test Questions. Answers are given at the end of the examination so that the student may evaluate his own work.

I. By equations, formulas, or words, show that you know what is meant by the following terms: (1) tautomerism, (2) electrophilic substitution, (3) S_N2 reaction, (4) molecular orbital, (5) vulcanization. 25 pts.

II. In a sentence or two, cite a contribution to organic chemistry made by five of the following named persons. If it is for a reaction, the equation for the reaction would serve best. (1) Markownikoff, (2) Friedel and Crafts, (3) Diels and Alder, (4) Von Baeyer, (5) Kekulé, (6) G. N. Lewis. 20 pts.

III. Pentalene has defied all attempts to synthesize it, presumably because it is too unstable. Its dianion, however, C_8H_6, forms a fairly stable salt which has been isolated. If the dianion is found to have aromatic character, what are two physical properties you would predict for it? 10 pts.



Pentalene

IV. What weight of crude zinc metal would be required to produce $\frac{1}{2}$ mole of $CH_3—CHOH—CHOH—CHNH_2—CH_3$ from $CH_3—CO—CO—CHNH_2—CH_3$ in acid solution if the zinc is only 90 per cent pure (assume that the impurity is inert) and if the reaction is only 80 per cent efficient? Zn = 65.4. 20 pts.

V. Starting with $Br—(CH_2)_6—Br$, what series of laboratory reactions would you use to prepare diaxial 1,2-cyclohexanediol? 20 pts.

VI. An unknown, optically active compound A, $C_9H_{12}O_3$, turns aq. ceric ammonium nitrate red, gives a red coloration with alc. $FeCl_3$, and gives a negative Lucas test. When 3.36 g of A are reacted with excess acetic anhydride, it requires 40 ml of 1 *N* NaOH to neutralize the liberated acetic acid. Reaction of A with dimethyl sulfate in alkali yields B, $C_{11}H_{16}O_3$, which when oxidized with potassium permanganate yields C, *p*-anisic acid, *p*-$CH_3O—C_6H_4—COOH$. 25 pts.

On the basis of this information, propose a structural formula for A and show how you deduced your answer.

VII. Make the following predictions:

1. Which would have the higher boiling point, *ortho-* or *meta*-chlorophenol?
2. Which would absorb ultraviolet light at the longer wavelength, *p*-nitroaniline or its hydrochloride salt?
3. Which compound should ionize to the greater extent in sulfuric acid, $(p\text{-}CH_3O—C_6H_4)_3—COH$ or $(p\text{-}O_2N—C_6H_4)_3—COH$?

Give the basis for your prediction in each case. 20 pts.

VIII. Given eight unlabeled bottles, each containing a different one of the following:

p-bromophenol
bromocyclohexane
1-heptyne
n-propyl ether
3-bromo-2-hexene
1-methylcyclohexanol
2-methylcyclohexanol
cyclohexene

Using qualitative test tube experiments only, how would you identify the contents of each bottle? 25 pts.

IX. Name one substance in list B which would be chosen for each use listed in column A.

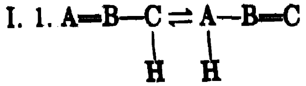
A. Uses	*B. Substances*
1. Aerosol bomb propellant	*p*-Dichlorobenzene
	Phenol
2. Insecticide	Iodoform
	Methanol
3. Anesthetic	Methyl bromide
	Buna S
4. Antiseptic	Vinyl chloride
	Butyl rubber
5. Solvent for grease	1080
	Carbon tetrachloride
6. Inner tube synthetic rubber	Freon
	Naphthalene
	Cyclopropane

5 pts.

X. What is a commercial source of each of the following: (a) methanol, (2) butadiene, (3) buna N rubber, (4) toluene, (5) glycerol, (6) phenol. 10 pts.

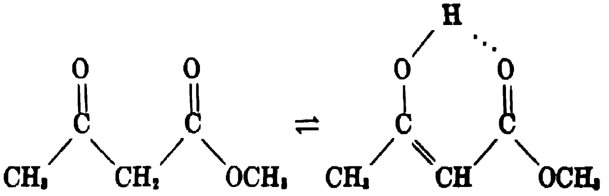
TOTAL SCORE 180 POINTS

ANSWERS TO THREE-HOUR EXAMINATION I

I. 1. 

$$\mathrm{A{=}B{-}\underset{\displaystyle H}{\underset{|}{C}} \rightleftharpoons \underset{\displaystyle H}{\underset{|}{A}}{-}B{=}C}$$

e.g.,



2. Reaction of an electron-seeking reagent, e.g.,

$$C_6H_6 + {}^+NO_2\ (HONO_2 + H_2SO_4) \rightarrow C_6H_5NO_2 + H^+$$

3. Substitution, nucleophilic, bimolecular:

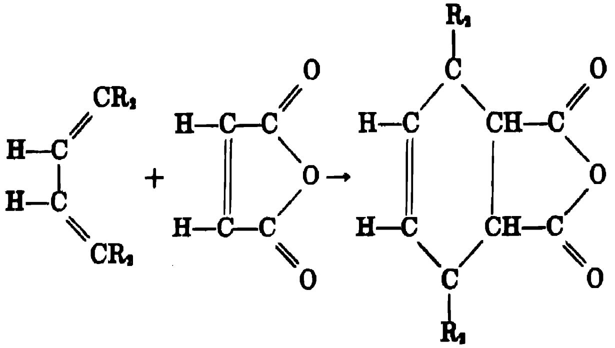
$$CH_3{-}CH_2Cl + OH^- \rightarrow CH_3{-}CH_2OH + Cl^-$$

4. The volume around the atomic framework of a molecule within which the electrons are most likely to be found.
5. The process of heating crude rubber with 5–8% of its weight of sulfur for several hours to produce a product with increased elasticity and less thermoplasticity.

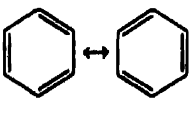
II. 1. Proposed generalization regarding the direction of addition of substances to C=C bonds; In the absence of oxygen or peroxides, the negative portion of an addendum will add to the carbon atom of an alkene to which there is attached the fewer number of carbon atoms.

2. $\phi{-}H + RX \xrightarrow{AlCl_3} \phi{-}R + HX$

3.



4. Bond-angle strain theory to account for olefinic character of cyclopropane; the use of aq. $KMnO_4$ to detect unsaturation.
5. The concept of the quadrivalence of carbon and multiple bonding between carbon, and the Kekulé structure of the benzene ring:

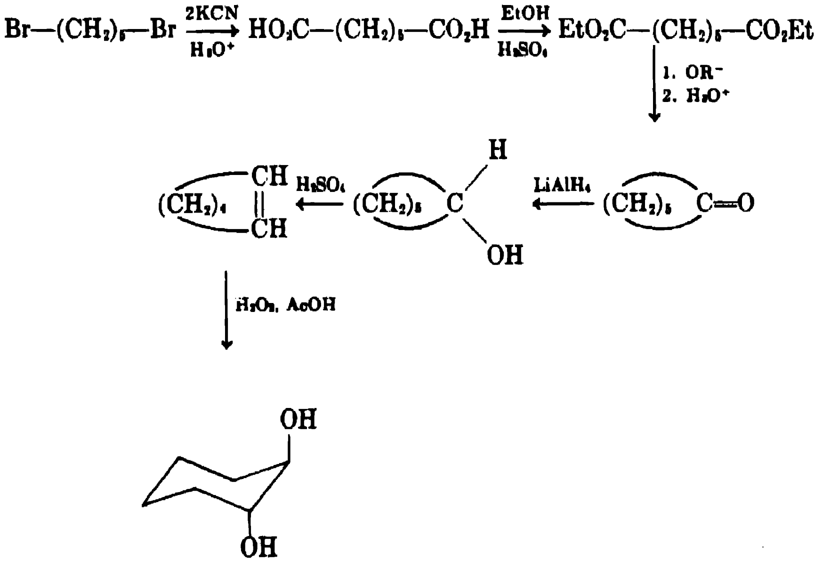


6. The octet theory of electron distributions around atoms, the concept of the covalent bond, and the electronic theory of acids and bases.

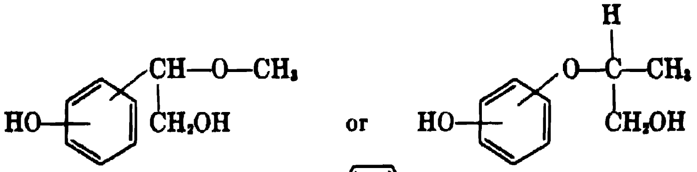
III. Would expect a planar ion, identical C—C bond lengths around the periphery, and n.m.r. proton signals near $\tau = 3.0$.

IV. 364 g.

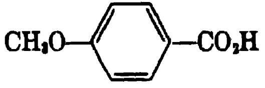
V.



VI. A = symmetric center; alcohol, phenol; primary alcohol; 2 OH's. Therefore,

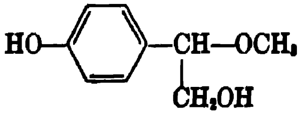


C =



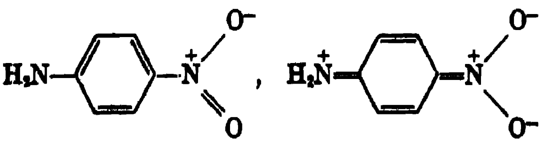
Therefore,

A =



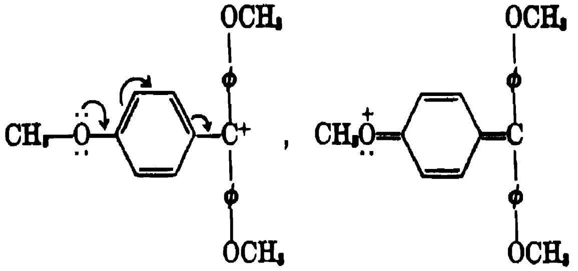
VII. 1. *m*-Chlorophenol, because it is associated, whereas the *ortho* isomer forms an intramolecular hydrogen bond and is not associated.

2. *p*-Nitroaniline, because there is the interaction resonance between the electron-releasing NH_2 group and the electron-withdrawing NO_2 group:



In the salt, the lone-pair electrons of the NH_2 group are tied up and the resonance above is blocked. The greater the resonance among these dipolar structures, the larger is λ_m.

3. The methoxy compound, because the methoxy group readily accepts the cationic charge; that is, the ion is a resonance hybird of the structures



Three equiv. forms involving each *p*-anisyl group

The nitro group does not accept the positive charge and therefore does not help stabilize the ion.

VIII. 1. $FeCl_3$ aq. identifies the *p*-bromophenol.

2. Test remaining bottles for the alcohols or for unsaturation, say, the alcohols with ceric ammonium nitrate. The two alcohols are then distinguished by the Lucas test; 1-methylcyclohexanol is a tertiary alcohol and would react in approximately half a minute.
3. Test remaining bottles for 1-alkyne with ammoniacal cuprous chloride to get precipitate with 1-hexyne.
4. Test for unsaturation with cold, alkaline permanganate; negative test with the bromocyclohexane identifies it. Treat samples of either of the two remaining bottles with aq. Ag^+ to get precipitate with the bromo compound which has allyl bromide structure. The other sample, then, is cyclohexene.
5. The ether is the only bottle to give negative tests to the classifying reagents, i.e., $FeCl_{3_{aq.}}$, Ce^{+4}, $Cu(NH_3)^+_2$, and MnO_4^-.

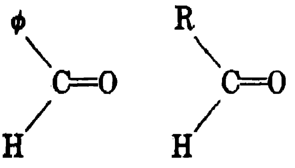
IX. 1. Freon
2. Naphthalene or *p*-dichlorobenzene
3. Cyclopropane
4. Iodoform
5. CCl_4
6. Butyl rubber

X. 1. Catalytic hydrogenation of CO
2. Cracking process
3. Copolymerization of $CH_2{=}CH{-}CH{=}CH_2$ plus $CH_2{=}CH{-}CN$
4. Coal tar and aromatization of *n*-heptane
5. Hydrolysis of fats or synthesis from propene
6. Coal tar, hydrolysis of chlorobenzene, or oxidation of isopropylbenzene to cumenehydroperoxide and rearrangement of the latter in sulfuric acid

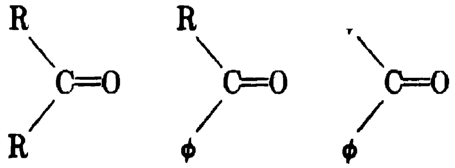
12

Aldehydes and Ketones

The aldehydes and ketones are the first classes of compounds to be taken up which contain a carbonyl group, C═O, in their structures. The aldehydes will always have at least one hydrogen atom attached to the carbonyl carbon atom and the ketones will have two groups joined to the carbonyl group.



Aldehydes

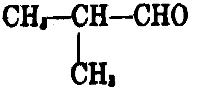


Ketones

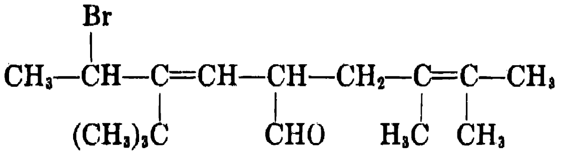
12.1 NOMENCLATURE

Under the Geneva system, the aldehyde class suffix is *-al* and the carbonyl carbon atom is regarded as the first in the chain. For example, the first three members of the aldehyde family are methanal, ethanal, and propanal, and CH_3—CHCl—CH_2—CHO is called *3-chlorobutanal.* Most of the short-chain aldehydes also have common names, derived from the names of the corresponding acids. When these trivial names are used, the carbon atoms are

TABLE 12.1. ALIPHATIC ALDEHYDE NOMENCLATURE

Structure	I.U.C. Name	Common Name
H—CHO	Methanal	Formaldehyde
CH_3—CHO	Ethanal	Acetaldehyde
CH_3CH_2—CHO	Propanal	Propionaldehyde
$CH_3CH_2CH_2$—CHO	Butanal	*n*-Butyraldehyde
$CH_3(CH_2)_3$—CHO	Pentanal	*n*-Valeraldehyde
 $CH_3-\underset{CH_3}{\underset{\vert}{CH}}-CHO$	2-Methylpropanal	α-Methylpropionaldehyde or isobutyraldehyde
CH_3—CHCl—CHCl—CHO	2,3-Dichlorobutanal	α,β-Dichlorobutyraldehyde

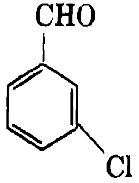
lettered according to letters of the Greek alphabet, beginning with the carbon atom attached to the carbonyl group. For illustration, the names of some aliphatic aldehydes are given in Table 12.1 according to both systems. The The I.U.C. system calls the aldehyde group a *formyl* group and the C=O group of a ketone *oxo* (commonly called *keto*). In some complex molecules, especially cyclic structures, it is simpler to regard these groups as substituents. For example,



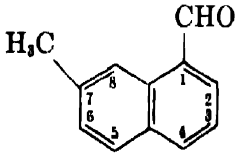
$$CH_3-\overset{\overset{Br}{|}}{CH}-\underset{\underset{(CH_3)_3C}{|}}{C}=CH-\underset{\underset{CHO}{|}}{CH}-CH_2-\underset{\underset{H_3C}{|}}{C}=\underset{\underset{CH_3}{|}}{C}-CH_3$$

can be named 2,3-dimethyl-5-formyl-7-*t*-butyl-8-bromo-2,6-nonadiene.

Aromatic aldehydes are named as derivatives of the parent hydrocarbon aldehydes which have common names. For example,



m-Chlorobenzaldehyde

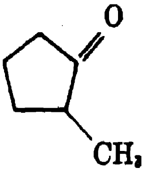


7-Methyl-1-naphthaldehyde

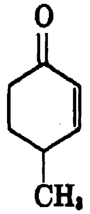
The class suffix for ketones is *-one*, and since there must be two carbon-attached groups joined to the carbonyl group, the smallest ketone is $CH_3-CO-CH_3$, and is named *propanone*. The carbon atoms in the chain are numbered, starting from the end nearest the carbonyl group. For illustration, $CH_3-CO-CH_2-CH(CH_3)-CH_3$ is named *4-methyl-2-pentanone*. When the two alkyl groups attached to the carbonyl group have simple names, the ketone may be named by naming the groups and adding the word *ketone*. Again, the carbon atoms in these groups are referred to by Greek alphabet lettering. Several examples of naming ketones are given in Table 12.2.

TABLE 12.2. KETONE NOMENCLATURE

Structure	I.U.C. Name	Common Name
$CH_3-CO-CH_3$	Propanone	Methyl ketone or acetone
$CH_3-CO-CH_2CH_3$	Butanone	Methyl ethyl ketone
$CH_3CH_2-CO-CH_2CH_3$	3-Pentanone	Ethyl ketone
$CH_3-CO-CH_2CH_2CH_3$	2-Pentanone	Methyl *n*-propyl ketone
$(CH_3)_2CH-CO-CHBrCH_2CH_3$	2-Methyl-4-bromo-3-hexanone	Isopropyl α-bromopropyl ketone
$CH_2BrCH_2-CO-CH_2CH_2Br$	1,5-Dibromo-3-pentanone	Bis-(β-bromoethyl) ketone

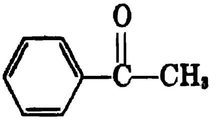


2-Methylcyclopentanone

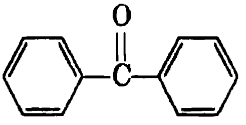


4-Methyl-2-cyclohexenone

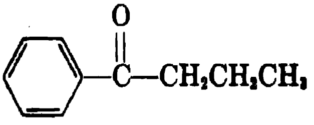
The simple aromatic ketones have common names which are regarded as acyl derivatives of a *phenone*. For example,



Acetophenone



Benzophenone



Butyrophenone

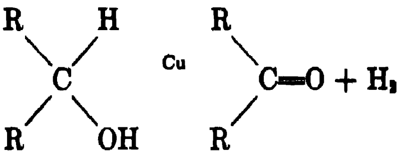
12.2 PREPARATION

a. Oxidation of alcohols. Primary alcohols may be oxidized to aldehydes and secondary alcohols to ketones.

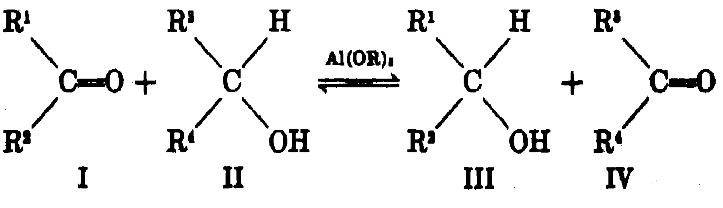
$$R\text{—}CH_2OH \xrightarrow{O.A.} RCHO \qquad O.A. = \text{dil. } Cr_2O_7^-,\ H_3O^+$$

$$R_2CHOH \quad ^{O.A.} \quad R_2CO \qquad Cu,\ \Delta$$

A common oxidizing agent for these oxidations is dilute potassium dichromate in acid solution. Concentrated solutions, or potassium permanganate, will tend to carry the oxidation beyond the aldehyde or ketone stages to yield carboxylic acids. The alcohols may be dehydrogenated, which is effectively an oxidation, by heating them with copper metal.

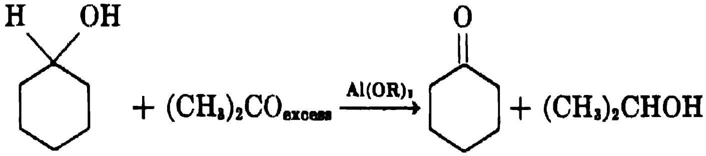


An effective method for bringing about these oxidations is the *Oppenauer oxidation*. In the presence of a specific type of catalyst, alcohols and carbonyl compounds undergo a reversible reaction as follows:



(1)

where the R's are numbered merely for reference. In effect, a carbonyl compound I is converted to its corresponding alcohol III, and an alcohol II is transformed to its corresponding carbonyl compound IV. The reaction is reversible, and in order to shift the equilibrium far to the right, one of the usual techniques of shifting equilibria may be employed. That is, either the molar ratio of one of the reactants is increased, or a product is removed as it is formed. For the present purpose of oxidizing an alcohol II to the corresponding carbonyl compound IV, acetone is used as the carbonyl compound I in equation (1), and a large ratio of I to II is obtained by using acetone as a solvent. The catalyst is an aluminum alkoxide, frequently aluminum isopropoxide which is commercially available. In the absence of the catalyst, the reaction does not take place. An illustration of this Oppenauer oxidation is as follows:

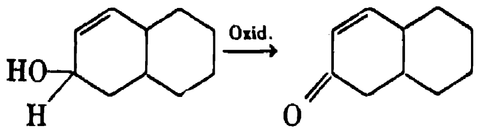


This reversible reaction may also be used for the preparation of alcohols by the reduction of the respective carbonyl compounds. That is, the objective in equation (1) may be to convert I to III. Such a reduction is called a *Meerwein-Ponndorf-Verley reaction* after the persons who contributed most to its development. In order to shift the equilibrium far to the right in this case, an alcohol II is used whose corresponding carbonyl compound IV is low-boiling and may be removed easily from the reaction mixture by distillation. Ethyl or isopropyl alcohols are normally used, for acetaldehyde and acetone have low boiling points (22° and 56°, respectively). Of course, the reaction is not used for the reduction of the first few simple ketones and aldehydes, whose boiling points are also low, because it is a simple matter to reduce them with the common reducing agents, such as iron in acetic acid, sodium amalgam, etc. Hence, the acetaldehyde or acetone products in a Meerwein-Ponndorf-Verley reduction will boil at much lower temperatures than the carbonyl compound being reduced. An example of the use of this reaction is the following:

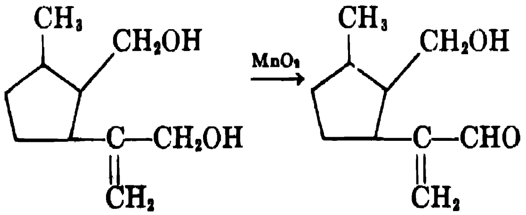
$$(CH_3)_2CHCH_2CH_2CH_2\text{—}CHO + (CH_3)_2CHOH \xrightarrow{Al(OR)_3} (CH_3)_2CHCH_2CH_2CH_2CH_2OH + (CH_3)_2CO$$

As a generalization, one can say that the Oppenauer oxidation consists of the oxidation of alcohols with acetone in the presence of an aluminum alkoxide catalyst, and the Meerwein-Ponndorf-Verley reduction consists of the reduction of aldehydes and ketones with ethyl or isopropyl alcohol in the presence of an aluminum alkoxide catalyst.

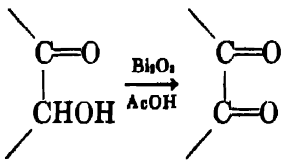
Another reagent that is quite specific for the oxidation of alcohol groups to the corresponding carbonyl compounds is a chromic anhydride-pyridine complex, $CrO_3:2C_5H_5N$. The advantage of these two oxidizing agents, CrO_3 in pyridine and acetone plus aluminum alkoxide, is that they may be used to oxidize selectively an alcohol group in the presence of an olefin group.



Aryl and allyl carbinols can be oxidized to the corresponding carbonyl compounds in good yields with MnO_2 or dimethylsulfoxide, $(CH_3)_2SO$. Thus, in a molecule containing an alkyl and an allyl alcohol group, the allyl alcohol group was selectively oxidized to an aldehyde group with MnO_2.



α-Keto alcohols, i.e., acyloins, R—CHOH—CO—R, can be smoothly oxidized to diketones with Bi_2O_3 in refluxing acetic acid.



A black precipitate of bismuth metal is quickly formed. The reaction is specific for α-keto alcohols, and even glucose gives a negative test.

b. Aldehydes and ketones from Grignard reagents.[2]

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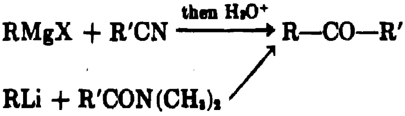
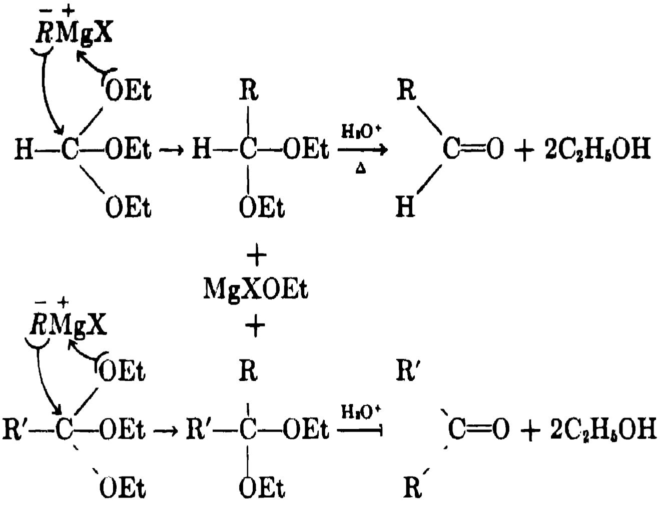
[2] Ketones can be prepared in good yields by the reactions



$$\begin{tikzcd} RMgX + R'CN \arrow[r, "\text{then } H_3O^+"] & R{-}CO{-}R' \\ RLi + R'CON(CH_3)_2 \arrow[ur] & \end{tikzcd}$$

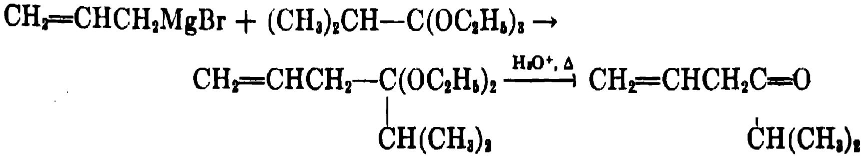
(Cf. P. T. Izzo and S. R. Safir, *J. Org. Chem.*, **24**, 701 (1959).



(2)

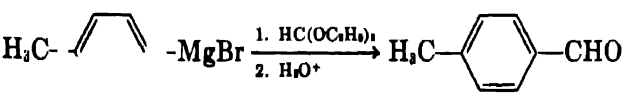
(3)

It will be recalled that the general formula for an ester is $\mathrm{R{-}\overset{\overset{OR}{|}}{C}{=}O}$. When two OR groups replace the carbonyl oxygen of an ester, giving $\mathrm{RC(OR)_3}$, the compound is called an *orthoester.* Since H—COOR is an alkyl formate, $\mathrm{H{-}C(OR)_3}$ is called an *orthoformate,* and hence, $\mathrm{H{-}C(OC_2H_5)_3}$ is ethyl orthoformate. $\mathrm{R'{-}C(OC_2H_5)_3}$ is merely a different ethyl orthoester whose R′ group will determine what ketone will be produced in reaction (3) with a Grignard reagent. So, for an aldehyde, a Grignard is reacted with ethyl orthoformate and for a ketone, a Grignard is reacted with a suitable orthoester. For illustration, isopropyl allyl ketone and tolualdehyde could be prepared as follows:

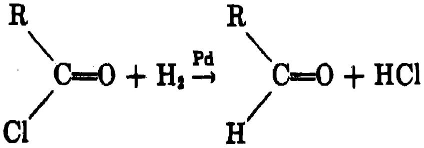


$$\mathrm{CH_2{=}CHCH_2MgBr + (CH_3)_2CH{-}C(OC_2H_5)_3 \rightarrow}$$

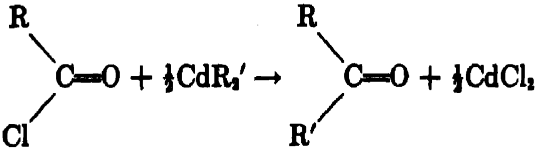
$$\mathrm{CH_2{=}CHCH_2{-}\underset{\displaystyle CH(CH_3)_2}{\underset{|}{C}}(OC_2H_5)_2 \xrightarrow{H_3O^+,\,\Delta} CH_2{=}CHCH_2\underset{\displaystyle CH(CH_3)_2}{\underset{|}{C}}{=}O}$$



c. Aldehydes and ketones from acid chlorides.



(4)



(5)

Reaction (4) is called the *Rosenmund reduction* and gives good yields in general. For reaction (5), the alkylcadmium is usually prepared by reacting cadmium bromide with the corresponding Grignard.

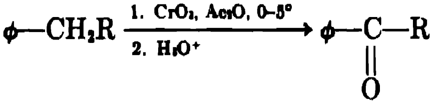
$$R'MgBr + \tfrac{1}{2}CdBr_2 \rightarrow \tfrac{1}{2}CdR_2' + MgBr_2$$

Secondary and tertiary alkyl halides generally give poor yields.

There are several methods used for preparing aromatic aldehydes and ketones which are not generally applicable in the aliphatic series. Five will be given here.

1. Oxidation of side-chain alkyl groups

$$\phi\text{—}CH_3 \xrightarrow[Ac_2O]{CrO_3, 0\text{–}5°} \phi\text{—}CH(OAc)_2 \xrightarrow{H_3O^+} \phi\text{—}CHO$$



$$\phi\text{—}CH_2R \xrightarrow[2.\ H_3O^+]{1.\ CrO_3,\ Ac_2O,\ 0\text{–}5°} \phi\text{—}\underset{\underset{O}{\|}}{C}\text{—}R$$

Chromium trioxide oxidizes C—H bonds to C—OH bonds, which are rapidly esterified to C—OAc bonds. A crystalline diacetate precipitates out of the reaction mixture, which inhibits further oxidation.

2. Hydrolysis of benzal halides

$$\phi\text{—}CHCl_2 + H_2O \xrightarrow[\Delta]{H_3O^+} \phi\text{—}CHO + 2HCl$$

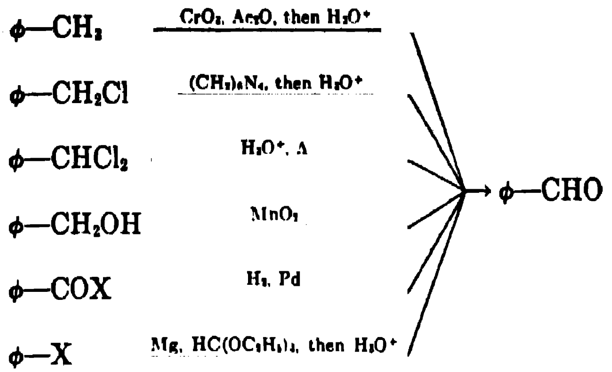
Substituted toluenes can be dihalogenated on the side chain, and the resulting benzal halides can be hydrolyzed in acid or mild alkali to the corresponding benzaldehydes. This is one of the principal commercial methods of producing benzaldehyde.

3. Sommelet reaction

$$\phi\text{—}CH_2X + (CH_2)_6N_4 \rightarrow \phi\text{—}CH_2\text{—}(CH_2)_6N_4^+X^- \xrightarrow{H_3O^+} \phi\text{—}CHO$$

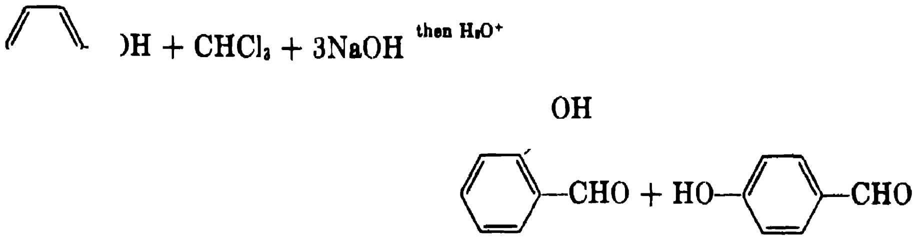
This reaction is simple to perform and good yields are generally obtained.

The chart on page 315 summarizes the methods given here for preparing aromatic aldehydes. Notice that a variety of functional groups can be transformed into the formyl group.



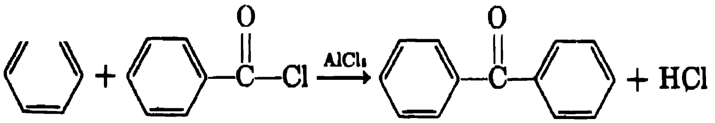
For hydroxy aldehydes, there is the Reimer-Tiemann reaction, discussed in Section 10.6f under the chemical properties of the phenols.

4. Reimer-Tiemann reaction

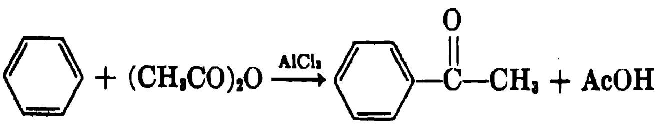


Aromatic ketones can be produced by an introduction of an acyl group into an aromatic nucleus by the Friedel-Crafts reaction.

5. Friedel-Crafts reaction



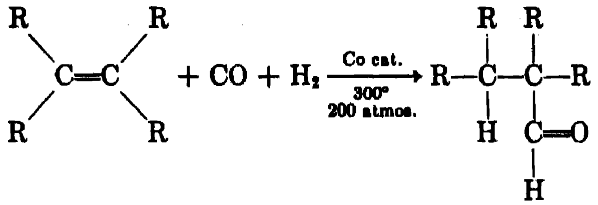
Benzophenone



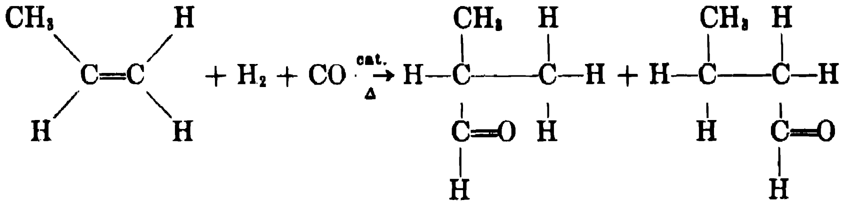
Acetophenone

Yields are not very high when there are *m*-orienting groups in the aryl nucleus.

In industry the aldehydes and ketones are normally produced by the catalytic air oxidation of the respective alcohols. There is one postwar method that has been developed, known as the OXO reaction. It consists of the addition of carbon monoxide and hydrogen to an alkene, i.e., *hydroformylation.*



Thus, propylene yields normal and isobutyraldehydes.



Isobutyraldehyde n-Butyraldehyde

12.3 PHYSICAL PROPERTIES

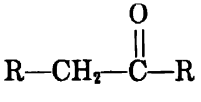
The structures of aldehydes and ketones lack OH groups for association through hydrogen bonding, and therefore, the compounds have lower boiling points (Table 12.3) than their corresponding alcohols. Only the first few members are completely water soluble—formaldehyde and acetaldehyde of the aldehydes, and acetone of the ketones—while methyl ethyl ketone is soluble to about 37 per cent.

TABLE 12.3. PHYSICAL CONSTANTS OF SOME ALDEHYDES AND KETONES

Name	*Melting Point*	*Boiling Point*
Formaldehyde	−92	−21
Acetaldehyde	−121	20
Propionaldehyde	−81	49
n-Butyraldehyde	−99	76
n-Valeraldehyde	−91	103
Crotonaldehyde	−77	104
Benzaldehyde	−26	178
p-Tolualdehyde		205
Salicylaldehyde	2	197
Anisaldehyde	3	248
Acetone	−94	56
Methyl ethyl ketone	−86	80
Methyl *n*-propyl ketone	−78	102
Diethyl ketone	−41	101
Cyclohexanone		157
Acetophenone	21	202
Propiophenone	21	218
Benzophenone	48	306

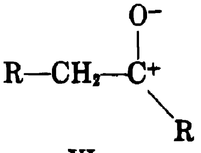
12.4 CHEMICAL PROPERTIES

As discussed in Section 7.2, whenever it is impossible to give a single structural formula for a compound which is consistent with all the observed properties, then chemists propose several logical structures, and regard the actual structure to be a weighted mean or composite of all the proposed structures. The proposed structures must differ merely by the positions of the electrons, and the situation is called *resonance*. Accordingly, the carbonyl group of ketones and aldehydes is believed to be a resonance hybrid of structures V and VI, plus others shown on page 323:



$R-CH_2-\overset{\overset{O}{\|}}{C}-R$

V

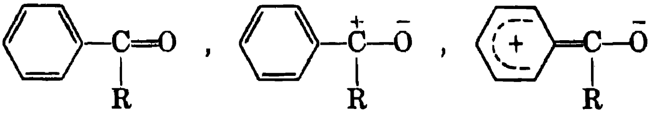


$R-CH_2-\overset{\overset{O^-}{|}}{C^+}-R$

VI

where the R's may be hydrogen atoms or carbon-attached groups. The relative importance of these structures is about 55 per cent for V to 40 per cent for VI. That is, aldehydes and ketones have a certain resemblance in behavior to structure VI. Justification for this view comes from the fact that most of the chemical properties of aldehydes and ketones can be accounted for in terms of structure VI and those shown on page 323. It will be observed that aldehydes and ketones undergo many addition reactions to the carbonyl group in which basic atoms (electron-pair donors) join the carbonyl carbon atom and acidic atoms (electron-pair acceptors) join the oxygen atom.

Aromatic aldehydes and ketones have the Kekulé resonance of the rings, the carbonyl group resonance, and a small interaction resonance between the ring and the carbonyl group:

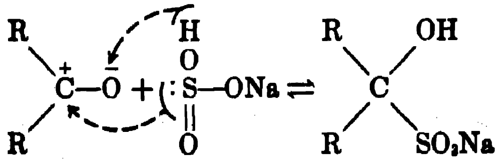


This makes the aromatic carbonyl compounds a little more stable than the aliphatic or alicyclic analogs.

Unless otherwise stated, the reactions discussed in this section apply to the aliphatic, alicyclic and aromatic series.

a. 1,2-Addition reactions.

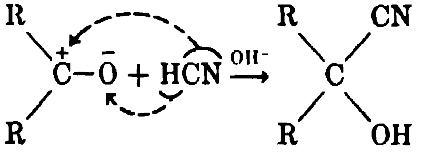
1. Sodium bisulfite:



Sodium bisulfite addition compound

The addition compound is a white, granular salt, and like most salts, if the aqueous sodium bisulfite solution used in the reaction is a saturated solution, the addition product will not dissolve in the saturated solution but will form a precipitate. The reaction, therefore, offers a convenient method of isolating aldehydes and methyl ketones or of removing them from a reaction mixture. The carbonyl compound may be recovered by decomposing the addition compound in dilute acid. It is to be noted that the reaction consists of an addition to the carbonyl group. Only aldehydes and methyl ketones give solid addition products because of a phenomenon called *steric hindrance*. The alkyl groups of a ketone, other than methyl groups, occupy so much space around the carbonyl carbon atom that they block the close approach of the bisulfite ion to the carbon atom for bond formation.

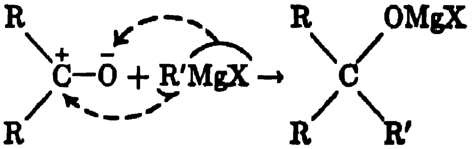
2. Hydrogen cyanide: In the presence of base, hydrogen cyanide adds to carbonyl compounds to yield *cyanohydrins*—compounds containing CN and OH groups:



A cyanohydrin

As will be seen later, the reaction offers a means of lengthening the carbon chain by a single carbon atom, because the CN group may be hydrolyzed to a COOH or $CONH_2$ group or reduced to a CH_2NH_2 group.

3. Grignard reagents: As stated previously, one of the typical reactions of Grignard reagents is to add to a C=O group.

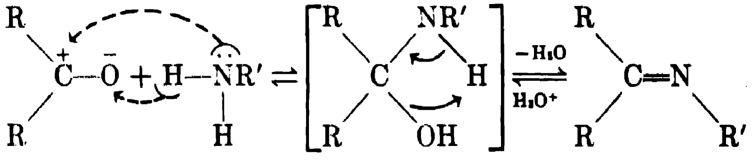


It will be recalled that this reaction is used in the preparation of alcohols (see Section 10.3).

In these three addition reactions the relative reactivity of carbonyl compounds decreases in the order $H_2C{=}O > RCHO > R_2CO$. This order is due to a steric effect in which the characteristic properties of a given class of compounds are *altered* for certain members owing to a spatial barrier about the atoms involved. For example, isopropyl ketone and hexamethylacetone,

$(CH_3)_3C{-}CO{-}C(CH_3)_3$, do not undergo any of these carbonyl addition reactions except the addition of hydrogen. The alkyl groups of these two ketones block the approach of the reagents to the carbonyl carbon atoms and thereby prevent addition from taking place. This can be seen more clearly by the use of models. Steric hindrance is an effect which will be encountered frequently and could be added to the list of differences between ionic and covalent substances (see Section 1.2). That is, steric hindrance is common among covalent organic reactions but rare among ionic inorganic reactions.

4. *Amines:* Primary amines react readily with carbonyl compounds to yield Schiff bases.



A Schiff base

The reaction proceeds by an addition to the double bond, but the intermediate addition compound loses water to give a Schiff base. The reaction is reversible, and, in the presence of acid, the carbonyl compound and amine salt may be recovered. This is a very useful reaction for the preparation of derivatives of aldehydes and ketones. Certain amines are more commonly used, and their names and the names of the corresponding Schiff bases are given in Table 12.4.

TABLE 12.4. THREE COMMON SCHIFF BASES*

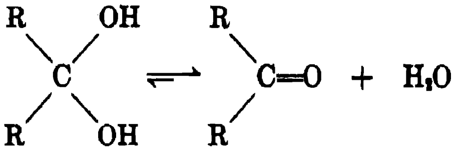
Amine		Schiff Base	
Hydroxylamine	H_2NOH	Oxime	$R_2C{=}NOH$
Phenylhydrazine	$H_2N{-}NHC_6H_5$	Phenylhydrazone	$R_2C{=}N{-}NHC_6H_5$
Semicarbazide	$H_2N{-}NHCONH_2$	Semicarbazone	$R_2C{=}N{-}NHCONH_2$

* A few others will be added to this list later.

This reaction with 2,4-dinitrophenylhydrazine to produce the corresponding 2,4-dinitrophenylhydrazone (2,4-DNP) is used as a qualitative test for an aldehyde or ketone. 2,4-DNP's, with few exceptions, are very slightly soluble in aqueous alcohol, so that the prompt formation of a yellow to red precipitate from the reaction medium is taken as a positive test. This test is one of the best of the functional group chemical tests because essentially all aldehydes and ketones give a positive test and rarely will any other functional group give a positive test.

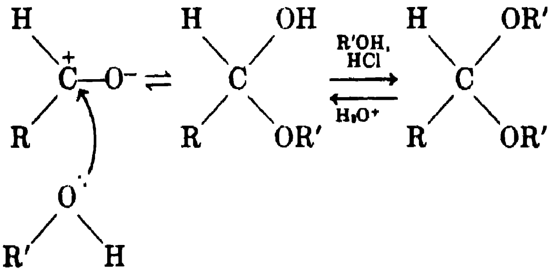
The C=N bond of Schiff bases is characterized by an infrared absorption band in the 1630–1690 cm^{-1} region.

5. *Hydrates:* We have used the generalization that molecules with two OH groups attached to a carbon gives an unstable species and that the molecule loses water to yield the carbonyl compound:



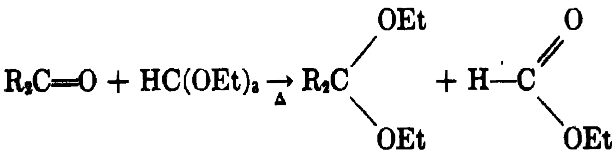
Actually there is a reversible equilibrium here which lies far over on the keto side. However, electronegative groups in R favor the hydrate side, and in water solution the compounds may exist as the hydrates. Such is the case for formaldehyde, perfluoroketones, and trihaloacetaldehydes, CX_3—CHO.

6. *Acetal formation:* Aldehydes react reversibly with alcohols to produce hemiacetals which react in the presence of acids to yield *acetals.*



Hemiacetal Acetal

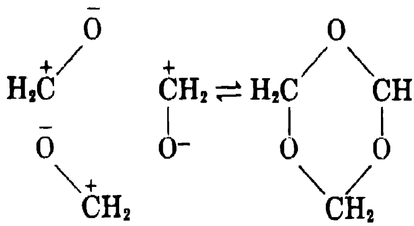
A hemiacetal is characterized by having an OH and an OR group attached to the same carbon atom, and an acetal has two OR groups joined to a single carbon. Thus, both compounds contain an ether linkage. Ordinarily the hemiacetals are not isolable as is the case with the aldehyde hydrates. The acetals can be prepared more conveniently by refluxing the carbonyl compounds with ethyl orthoformate.



$$R_2C{=}O + HC(OEt)_3 \xrightarrow[\Delta]{} R_2C(OEt)_2 + H{-}C({=}O)OEt$$

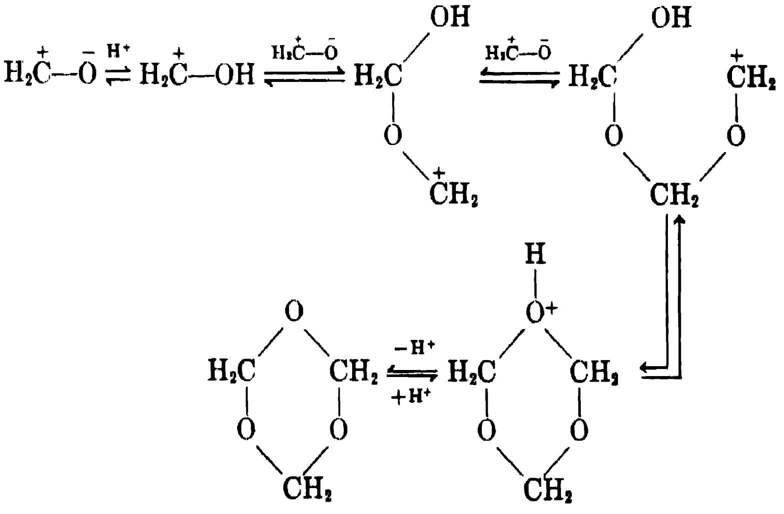
Acetals are easily hydrolyzed to the carbonyl compounds in dilute acid but not in basic media. Thus, they offer protection to carbonyl compounds from the various base-catalyzed condensations (to be discussed later in this chapter) when some other reaction is to be carried out in a basic medium. For example, one may want to perform a base-catalyzed dehydrohalogenation or nucleophilic displacement reaction on a halogenated ketone. In this case, the acetal could be prepared, the dehydrohalogenation carried out in base, then the carbonyl group regenerated by hydrolysis of the acetal in dilute acid solution.

b. Polymerization of aldehydes. Formaldehyde slowly condenses to a trimer and a polymer upon standing.



Trioxane
B.p. = 115°; m.p. = 62°

Strong acids partially stabilize the ionic form of the aldehyde, and thus catalyze the reaction.



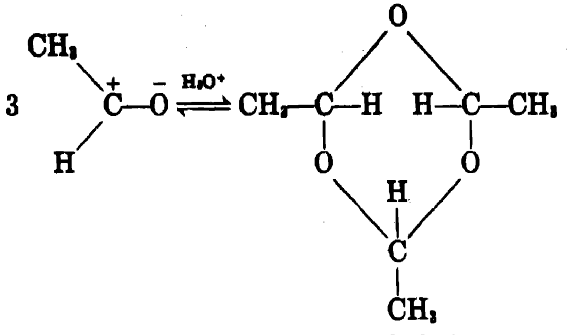
Trioxane

$$n\ H_2C{=}O \rightleftharpoons (H_2CO)_n$$

Paraformaldehyde

The reaction is catalyzed in both directions by acid. When the condensation product is heated in the presence of a trace of acid and the liberated formaldehyde distilled as it is formed, the equilibrium is shifted toward the monomer. Thus, trioxane and paraformaldehyde serve as convenient sources of dry formaldehyde.

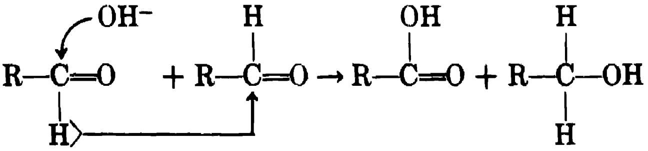
Acetaldehyde also condenses to a definite product, called *paraldehyde.*



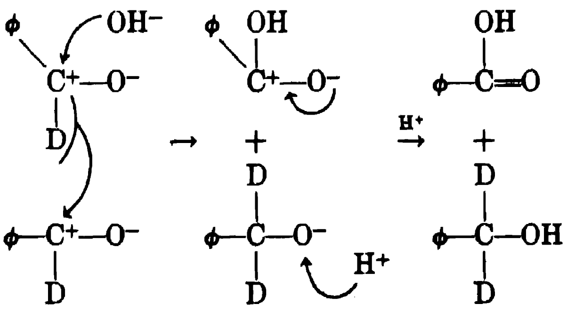
Paraldehyde
B.p. = 124°

Paraldehyde is commercially available and serves as a source of pure acetaldehyde. These condensation products are sparingly soluble in water and show no characteristic aldehyde reactions. Higher aldehydes polymerize to a small extent, but do not yield definite isolable products.

c. Cannizzaro reaction. The Cannizzaro reaction consists of the transfer of a hydride ion from one carbonyl group to another.



The reaction is promoted by a nucleophilic attack of hydroxide ion on the first carbonyl group and aided by a withdrawal of the hydride ion by the electrophilic carbonyl carbon of the second aldehyde. Evidence for this mechanism of the reaction is found in the use of a deuteroaldehyde:

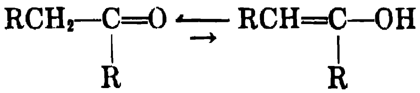


Hence, the alcohol is found to contain two deuterium atoms, one being the initial aldehydic deuterium and the second by transfer from the other aldehyde molecule. The reaction can be expressed by the following equation, in which it can be seen that one molecule of aldehyde is oxidized to the acid level and one is reduced to the alcohol level:

$$2RCHO + OH^-_{conc.} \rightarrow RCO_2^- + RCH_2OH$$

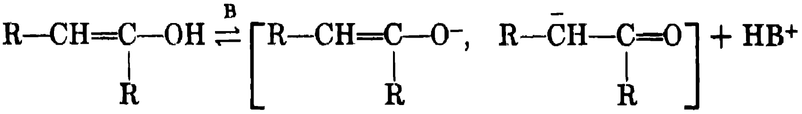
The Cannizzaro reaction is only used with aldehydes lacking an alpha hydrogen atom, for otherwise, a faster reaction would take place, such as described in the next section.

d. Base-catalyzed condensations. The keto-enol equilibrium of simple aldehydes and ketones,



$$RCH_2{-}\underset{\displaystyle R}{\underset{|}{C}}{=}O \rightleftharpoons RCH{=}\underset{\displaystyle R}{\underset{|}{C}}{-}OH$$

lies far to the left; but since the enol is the stronger acid, the presence of base shifts the equilibrium to the right through neutralization,

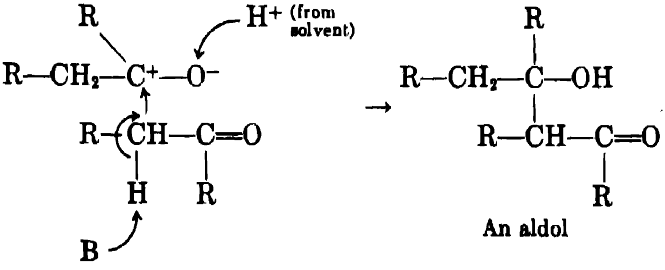


$$R{-}CH{=}\underset{\displaystyle R}{\underset{|}{C}}{-}OH \overset{B}{\rightleftharpoons} \left[R{-}CH{=}\underset{\displaystyle R}{\underset{|}{C}}{-}O^-,\quad R{-}\bar{C}H{-}\underset{\displaystyle R}{\underset{|}{C}}{=}O\right] + HB^+$$

VII VIII

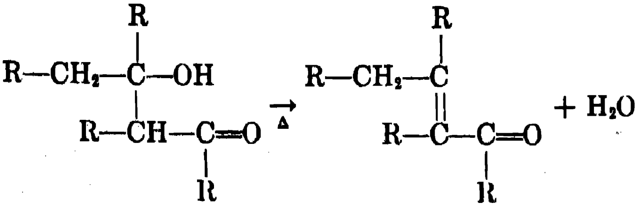
where B is a base. The enolate ion is a resonance hybrid of the two structures VII and VIII, which gives the α-carbon atom a partial anionic character. It thereby may react with the cationic carbonyl carbon atom of another molecule.

Accordingly, several classes of compounds with a CH group alpha to a C=O or NO_2 group (esters Section 15.5; nitroalkanes Section 16.4) condense with aldehydes and ketones in the presence of a base, including aldehydes and ketones themselves. One such reaction is the *aldol condensation:*



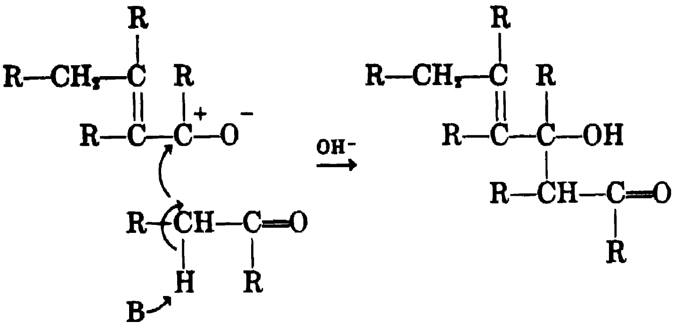
An aldol

Observe that it is the α-carbon of one molecule adding to the carbonyl carbon of the other molecule. In concentrated alkali, or upon heating the dilute alkaline solution, the aldol loses a molecule of water.



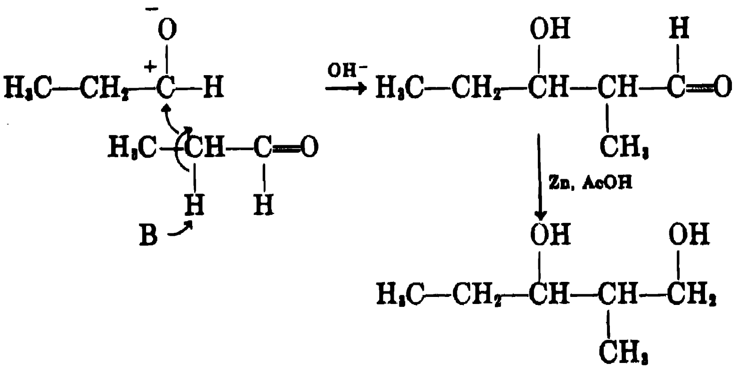
$$R{-}CH_2{-}\overset{\displaystyle R}{\overset{|}{C}}{-}OH \;\Big|\; R{-}CH{-}\underset{\displaystyle R}{\underset{|}{C}}{=}O \xrightarrow{\Delta} R{-}CH_2{-}\overset{\displaystyle R}{\overset{|}{C}} \;\|\; R{-}C{-}\underset{\displaystyle R}{\underset{|}{C}}{=}O + H_2O$$

In these structures, any one or all of the R's may be hydrogen atoms. Since the product still has a carbonyl group in it, more of the original ketone or aldehyde may add as it did initially.



Thus, this reaction can occur over and over to give a resin with large molecular weight. Although it is a slow reaction, chemists still avoid prolonged contact of aldehydes and ketones with alkali, to prevent loss of material through this reaction. This aldol condensation cannot take place if there are no hydrogen atoms on the α-carbon atom. Instead, the Cannizzaro reaction takes place.

Aldols serve as easy sources of 1,3-glycols, because the carbonyl group can easily be reduced to an alcohol group. For illustration, 2-methyl-1,3-pentanediol could be prepared from propionaldehyde:



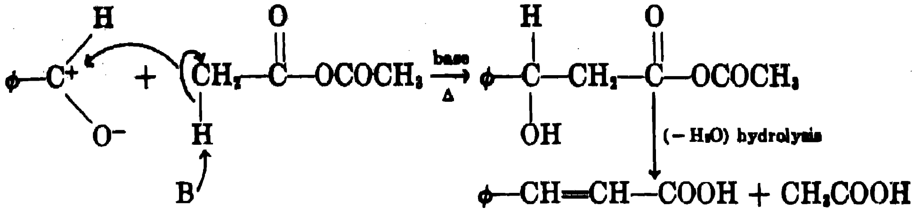
The glycols could then be dehydrated to various types of dienes.

Perkin reaction:

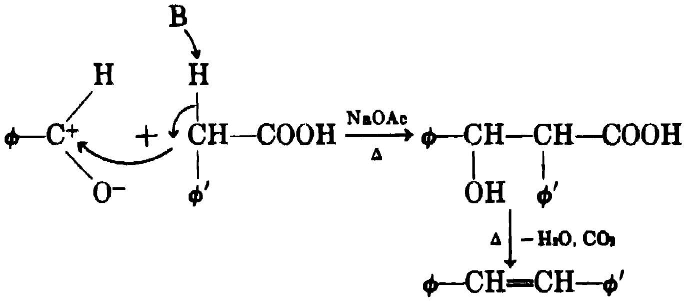
$$\phi\text{—CHO} + (CH_3CO)_2O \xrightarrow[\Delta]{\text{base}} \phi\text{—CH=CH—COOH}$$

Base = AcONa or R_3N

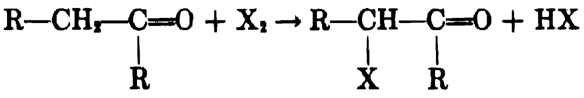
In the presence of a mild base and at elevated temperatures (*ca.* 150°), the anhydride undergoes an aldol-type condensation with aldehydes to yield α,β-unsaturated acids.



The reaction can be used with other active methylene groups as well:

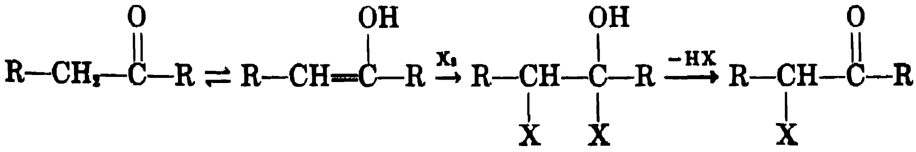


e. Halogenation. Aldehydes and ketones readily undergo polar halogenation at the α-carbon atoms:



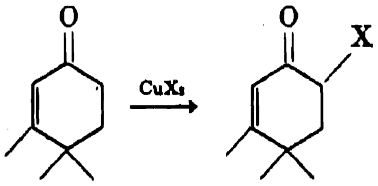
$$R\text{—}CH_2\text{—}\underset{\underset{\displaystyle R}{|}}{C}\text{=}O + X_2 \rightarrow R\text{—}\underset{\underset{\displaystyle X}{|}}{CH}\text{—}\underset{\underset{\displaystyle R}{|}}{C}\text{=}O + HX$$

In the presence of peroxides, a free radical halogenation can occur any place in the chain (Section 2.7d), but under polar conditions, the halogenation is limited to the α-carbons wherein the reaction takes place by addition to the enol form of the carbonyl compound.

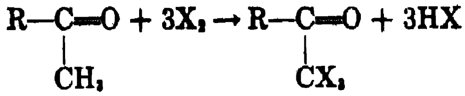


$$R\text{—}CH_2\text{—}\overset{\overset{\displaystyle O}{\|}}{C}\text{—}R \rightleftharpoons R\text{—}CH\text{=}\overset{\overset{\displaystyle OH}{|}}{C}\text{—}R \xrightarrow{X_2} R\text{—}\underset{\underset{\displaystyle X}{|}}{CH}\text{—}\overset{\overset{\displaystyle OH}{|}}{\underset{\underset{\displaystyle X}{|}}{C}}\text{—}R \xrightarrow{-HX} R\text{—}\underset{\underset{\displaystyle X}{|}}{CH}\text{—}\overset{\overset{\displaystyle O}{\|}}{C}\text{—}R$$

Cupric halide salts serve as useful halogenating agents, because unsaturated carbonyl compounds can be halogenated without affecting the olefin bond and phenols can be monohalogenated.

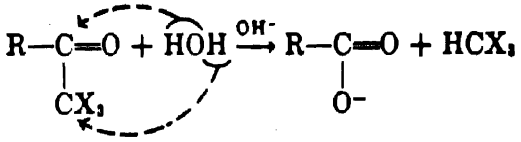


α-Halocarbonyl compounds are usually lachrymators, and for years the standard lachrymator in tear gas was α-chloroacetophenone, $C_6H_5COCH_2Cl$. More than one alpha hydrogen may be replaced, and in fact, the reaction speeds up as α-hydrogens are progressively substituted by halogens.



$$\mathrm{R{-}\underset{\underset{\displaystyle CH_3}{|}}{C}{=}O + 3X_2 \rightarrow R{-}\underset{\underset{\displaystyle CX_3}{|}}{C}{=}O + 3HX}$$

In alkali, the —CX_3 group is easily cleaved off to yield a haloform:

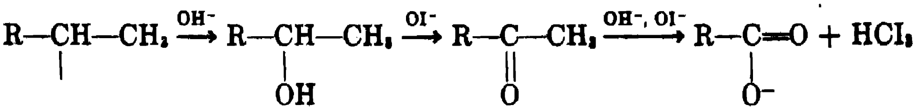


$$\mathrm{R{-}\underset{\underset{\displaystyle CX_3}{|}}{C}{=}O + HOH \xrightarrow{OH^-} R{-}\underset{\underset{\displaystyle O^-}{|}}{C}{=}O + HCX_3}$$

This reaction forms the basis of a method for the qualitative detection of methyl ketones. Iodine is employed for the test, in which case iodoform is produced. Iodoform is a pale yellow solid (white, when in a fine crystalline form) and its formation is readily recognized. It will be recalled that in aqueous alkali, the halogens, except fluorine, exist as halide plus hypohalite ions.

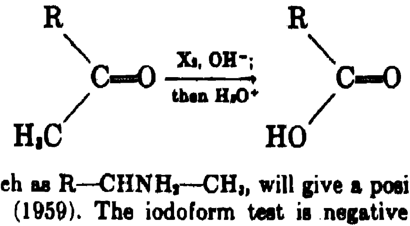
$$X_2 + 2(OH^-) \rightarrow X^- + OX^- + H_2O$$

The hypohalite ions are halogenating agents as well as being mild oxidizing agents. So, when a sample is warmed with an aqueous, alkaline solution of iodine, the appearance of iodoform is taken as an indication of a methyl ketone, or a substance transformable into a methyl ketone under these conditions.[3] For instance, acetaldehyde, methylcarbinols, and the corresponding halides give positive iodoform tests, because under the conditions of the reaction, the alkyl halides hydrolyze to the respective methylcarbinols, and the latter are oxidized by the hypoiodite ion to a methyl ketone which then yields iodoform.



$$\mathrm{R{-}\underset{|}{CH}{-}CH_3 \xrightarrow{OH^-} R{-}\underset{\underset{\displaystyle OH}{|}}{CH}{-}CH_3 \xrightarrow{OI^-} R{-}\underset{\underset{\displaystyle O}{\|}}{C}{-}CH_3 \xrightarrow{OH^-,\,OI^-} R{-}\underset{\underset{\displaystyle O^-}{|}}{C}{=}O + HCI_3}$$

The reaction is almost quantitative and can be used as a method of converting a methyl ketone to a carboxylic acid of one fewer carbon atoms.



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[3] Other compounds, such as R—$CHNH_2$—CH_3, will give a positive test (cf. B. T. Gillis, *J. Org. Chem.*, **24**, 1027 (1959). The iodoform test is negative for compounds such as CH_3CO—CH_2CO_2R, CH_3CO—CH_2NO_2, and CH_3CO—CH_2CN, in which the acyl group is easily cleaved by the reagent to acetic acid, and the latter compound resists polyhalogenation. For a discussion of the mechanism of the haloform reaction, see R. N. Seelye and T. A. Turney, *J. Chem. Educ.*, **36**, 572 (1959).

The carbonyl oxygen atom of aldehydes and ketones may be replaced by two halogen atoms through reaction with PCl_5.

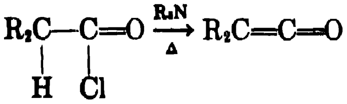
$$R_2C=O + PCl_5 \rightarrow R_2CCl_2 + POCl_3$$

The *gem*-dihalides may serve for the preparation of alkynes upon treatment with $KOH_{alc.}$ or $NaNH_2$

$$R-CH_2-CCl_2-R \xrightarrow{KOH_{alc.}} R-C\equiv C-R$$

$$R-CH_2-CHCl_2 \xrightarrow{NaNH_2;\ \text{then}\ H_3O^+} R-C\equiv C-H$$

f. **Ketenes.** Ketenes are unsaturated ketones in which the carbonyl carbon also forms the olefinic bond, $R_2C=C=O$. They can be prepared by the dehydrohalogenation of acid chlorides:

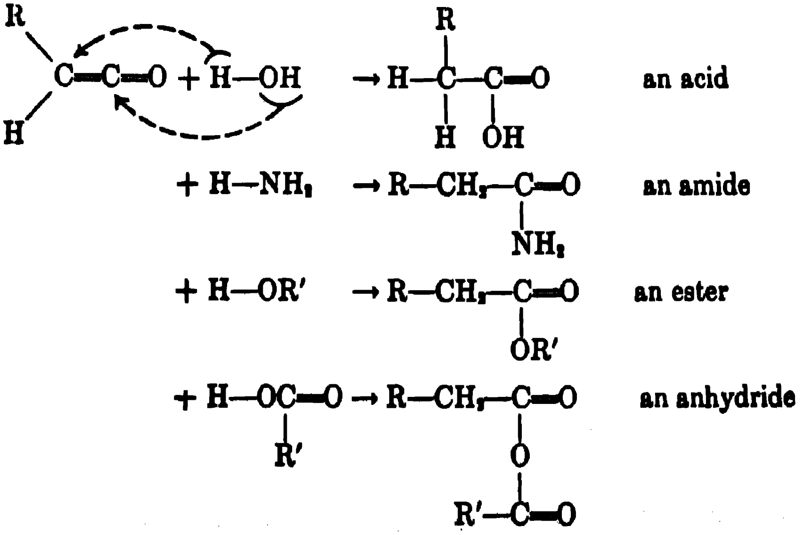


$$\underset{\substack{|\\ H}}{R_2C}-\underset{\substack{|\\ Cl}}{C}=O \xrightarrow[\Delta]{R_3N} R_2C=C=O$$

The first member, ketene, can also be made through the pyrolysis of acetone.

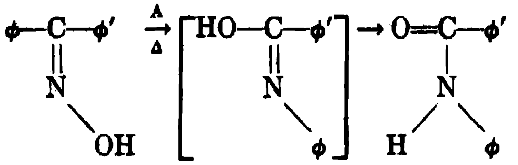
$$CH_3-CO-CH_3 \xrightarrow[\Delta]{500^\circ} CH_2=C=O$$

Ketenes are extremely reactive and polymerize or add compounds containing an active hydrogen atom very rapidly.



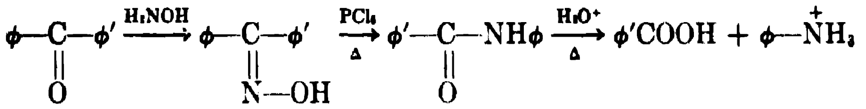
This last reaction is used for the commercial production of acetic anhydride from ketene (from acetone) and acetic acid.

g. Beckmann rearrangement.

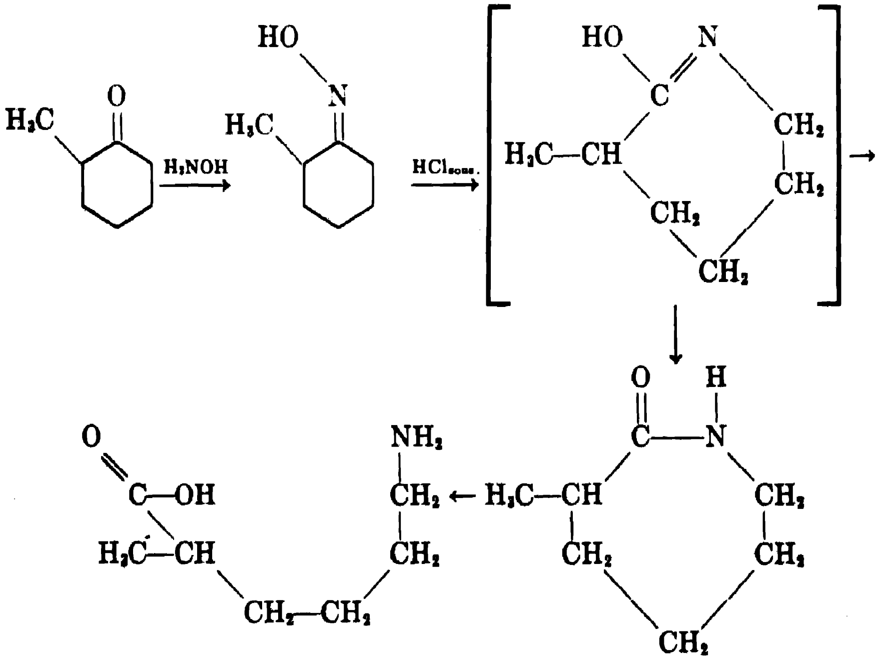


A = PCl_5, H_2SO_4, or ϕSO_2Cl

Ketoximes rearrange to give substituted amides when heated in the presence of one of the given catalysts. It has been established that the rearrangement involves the group which is *trans*[4] to the OH (in the above equation, φ and OH exchanged places), and this fact is sometimes used to determine the stereo structure of an oxime. The reaction is used also as a means of cleaving ketones or of opening a ring through the series of reactions:



$$\phi\!-\!\underset{\underset{O}{\|}}{C}\!-\!\phi' \xrightarrow{H_2NOH} \phi\!-\!\underset{\underset{N-OH}{\|}}{C}\!-\!\phi' \xrightarrow[\Delta]{PCl_5} \phi'\!-\!\underset{\underset{O}{\|}}{C}\!-\!NH\phi \xrightarrow[\Delta]{H_3O^+} \phi'COOH + \phi\!-\!\overset{+}{N}H_3$$



Aldoximes may undergo the rearrangement, but they tend to give considerable amounts of dehydration products.

h. Reduction and oxidation of aldehydes and ketones. Aldehydes and ketones are very easily reduced to the corresponding alcohols.

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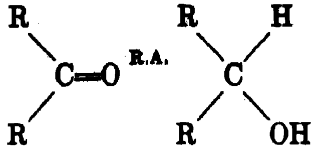
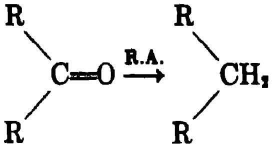
[4] With oximes, the terms *syn-* and *anti-* are used instead of *cis-* and *trans-*.



R.A. = H_2 + cat.
NaHg
Fe in AcOH
$LiAlH_4$
Meerwein-Ponndorf-Verley reduction

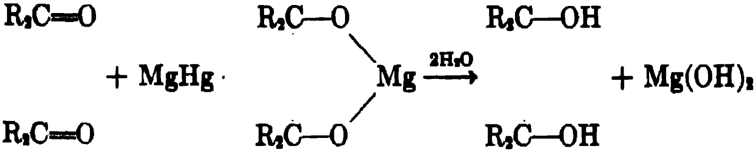
The reduction of aldehydes or ketones all the way to hydrocarbons can also be done.



R.A. $ZnHg_x$ + HCl
$H_2N—NH_2$ + OR^-
H_2 + cat.

The use of amalgamated zinc in hydrochloric acid, known as the *Clemmensen reaction*, has found wide application. The *Wolff-Kishner* method employs hydrazine with a sodium ethoxide catalyst at 180° and is used, usually, when the Clemmensen reaction cannot be used. Such instances would be when the carbonyl compounds are unstable in acids.

With mild reducing agents, such as magnesium amalgam, ketones (rarely aldehydes) undergo a reduction and condensation to yield pinacols, i.e., 1,2-glycols.

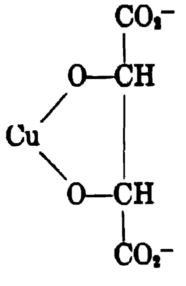


The molecular rearrangement of pinacols to pinacolones when heated in dilute acid was pointed out in Section 10.8.

Aldehydes are more easily oxidized than ketones, and mild oxidizing agents such as cupric and silver ions are sufficiently strong in alkaline media to oxidize the aldehydes selectively. Since these ions would immediately precipitate as the hydroxides or oxides in alkaline solution, they are used in the form of soluble complexes. Tollens' reagent is an ammoniacal solution of silver nitrate in which the silver ion exists as the ammonia complex. This will oxidize aldehydes to the corresponding carboxylic acids.

$$RCHO + 2Ag(NH_3)_2^+ + 3OH^- \rightarrow RCO_2^- + 2Ag + 4NH_3 + 2H_2O$$

The metallic silver forms as a black colloidal precipitate or as a shiny mirror coating on the glass walls of the vessel. Tollens' reagent will not oxidize ketones and if kept cold, will not oxidize alcohols. Fehling's solution is a tartaric acid complex of cupric ion.

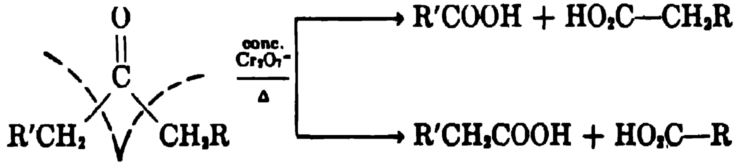


It is not as strong an oxidizing agent as Tollens' reagent and must be heated to bring about the oxidation of aldehydes to the respective acids.

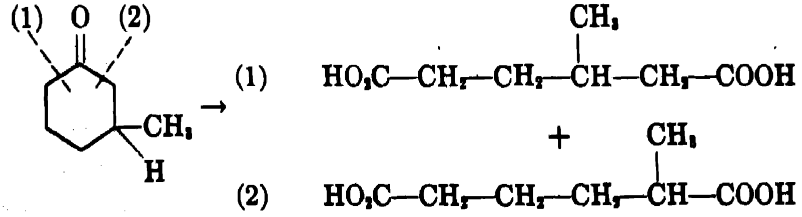
$$RCHO + 2Cu^{++} + 5OH^- \rightarrow RCO_2^- + 3H_2O + Cu_2O$$

The cuprous oxide appears as a yellow to red precipitate. Other complexes of copper are used too; for example, the citric acid complex is used in Benedict's solution, and the ethylenediaminetetraacetic acid (page 475) complex has been used. The oxidation potential of the copper in Benedict's solution is just the right value to oxidize aliphatic aldehydes but not aromatic aldehydes. Thus, it can be used generally to distinguish the two types of aldehydes.

The oxidation of ketones involves the cleavage of the carbon bonds to the carbonyl group to yield two possible acids each with fewer carbon atoms,

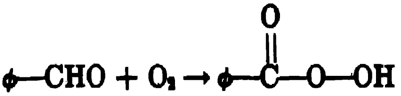


or, in the case of an alicyclic ketone, ring opening occurs:



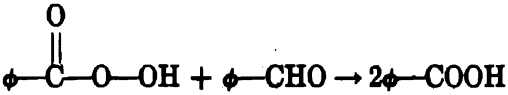
Auto-oxidation: Upon standing in open bottles or frequently opened bottles, many aromatic aldehydes slowly change to the corresponding benzoic acids. Since there is no apparent chemical oxidizing agent, this has been called *auto-*

oxidation (self-oxidation). However, oxygen of the air is really the oxidizing agent.



$$\phi\text{—CHO} + O_2 \rightarrow \phi\text{—}\overset{O}{\overset{\|}{C}}\text{—O—OH}$$

Perbenzoic acid

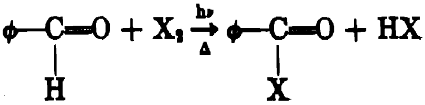


$$\phi\text{—}\overset{O}{\overset{\|}{C}}\text{—O—OH} + \phi\text{—CHO} \rightarrow 2\phi\text{—COOH}$$

Oxygen converts benzaldehyde to perbenzoic acid, which then oxidizes a second molecule of benzaldehyde to benzoic acid. The net change, then, is for two moles of benzaldehyde in air to give two moles of benzoic acid. If there is some other substance present, the perbenzoic acid may oxidize it instead of a benzaldehyde molecule. This is actually used as a preparative method of making glycols from olefins.

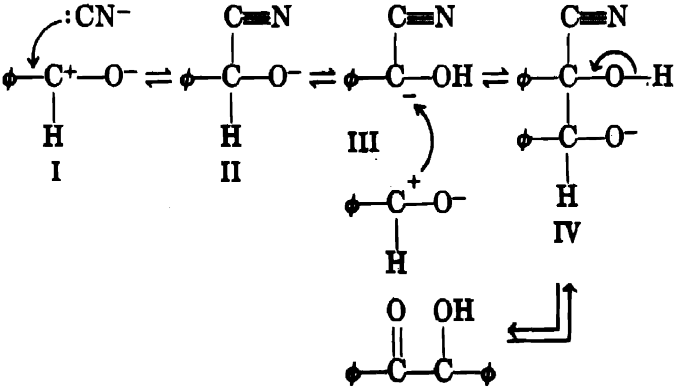
As can be expected, the aromatic aldehydes and ketones undergo some reactions attributable to the presence of an aromatic nucleus:

Side-chain halogenation:



$$\phi\text{—}\underset{H}{\underset{|}{C}}\text{=O} + X_2 \xrightarrow[\Delta]{h\nu} \phi\text{—}\underset{X}{\underset{|}{C}}\text{=O} + HX$$

Benzoin condensation: Aldehydes condense to form benzoins in the presence of cyanide ion, which is one of the rare catalysts for this reaction.



Benzoin

The effectiveness of cyanide ion is due to its ease of addition to the carbonyl group of I, its electron-withdrawing power in II to promote expulsion of a proton in II to give III, and its leaving power in IV.

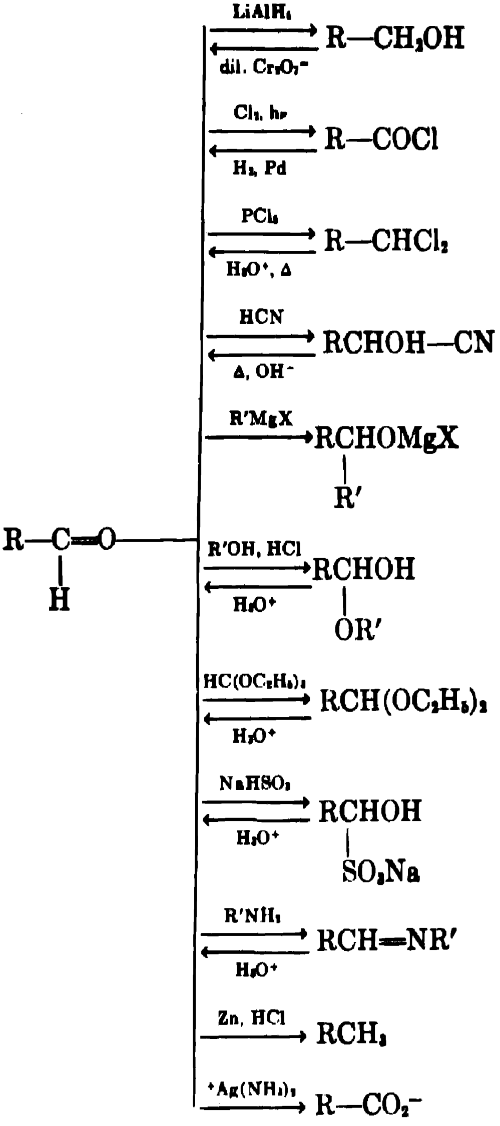


Fig. 12.1. Characteristic reaction chart for aldehydes.

12.5 USES OF ALDEHYDES AND KETONES

Formaldehyde is a powerful germicide and antiseptic, and finds wide application in disinfecting, sterilizing, and embalming processes. It is used in large amounts for the production of certain plastics like Bakelite. Acetone is used extensively as a solvent, because it is completely miscible with water and dissolves many organic compounds. Methyl ethyl ketone is used by the paint industry as a solvent for lacquers. The high-molecular-weight aldehydes and ketones usually have pleasant odors at low concentrations, and are used in perfumes.

STUDY EXERCISES

1. Give three general equations for the preparation of aliphatic aldehydes or ketones.

2. Indicate reactions one would use to prepare (a) *n*-propyl ketone and (b) hexanal.

3. Write balanced equations for the following reactions:

(a) $CH_3CH_2—CO—CH_3 + C_2H_5MgBr \rightarrow$
$CH_3CH_2—CO—CH_3 + HCN \rightarrow$
$CH_3CH_2—CO—CH_3 + H_2NOH \rightarrow$
(b) Heptanal + phenylhydrazine →
(c) The formation of the semicarbazone of ethyl ketone.

4. Write structural formulas for (a) 3-methyl-4-heptanone, (b) bis-(α-bromopropyl) ketone, (c) β-methylvaleraldehyde.

5. How would one reduce $(CH_3)_2CH—CH{=}CH—CHO$ to the corresponding alcohol and $(CH_3CH_2CH_2)_2CO$ to $(CH_3CH_2CH_2)_2—COH—COH—(CH_2CH_2CH_3)_2$?

6. How would one oxidize $CH_3CH{=}CHCH_2OH$ to $CH_3CH{=}CHCHO$?

7. Illustrate by equations: (a) the aldol condensation of butyraldehyde, (b) the reaction of trimethylacetaldehyde in conc. alkali, (c) the addition of sodium bisulfite to γ-methylvaleraldehyde.

8. Write a balanced equation for the oxidation of hexanal with Tollens' reagent.

9. How could acetaldehyde be used as a source of compounds with a four-carbon chain?

10. Give equations for the following:

(a) The preparation of *p*-chlorobenzaldehyde from the respective toluene, benzyl alcohol, benzal chloride, and benzyl bromide.
(b) The Perkin reaction.
(c) The benzoin condensation.
(d) The Cannizzaro reaction.
(e) The Beckmann rearrangement.
(f) The preparation of acetophenone from benzene with acetyl chloride, or with acetic anhydride.
(g) The reaction of acetophenone with hydrogen cyanide, hydroxylamine, and with phenylhydrazine.

11. Give structural formulas for the compounds in the following reactions:

$$\begin{tikzcd}
CO_2K—CH_2—C(CH_3)_2—CO_2Et \arrow[rrr, "\text{electrolysis}"] & & & C_{14}H_{26}O_4 + 2CO_2 \arrow[d, "\text{Na, xylene, then } H_3O^+"] \\
& C_{10}H_{18} & C_{10}H_{20}O \arrow[l, "H_2SO_4", "\Delta"'] & C_{10}H_{18}O_2 \arrow[l, "H_2N—NH_2", "\text{NaOEt, } 180^\circ"']
\end{tikzcd}$$

12. Give a laboratory synthesis of $C_6H_5CH{=}CHCH_3$ starting with benzyl bromide.

TEST QUESTIONS, Set 12

1. Five unlabeled liquids are known to be ethyl bromide, ethyl ether, *n*-hexane, butyraldehyde, and acetone. How could one proceed to label each?

2. How could the following be distinguished by qualitative test-tube experiments: (a) heptanal from *n*-heptanol, (b) hexanal from 2-hexanone, (c) 2-hexanol from 3-hexanol, (d) acetone from 2-pentanone, (e) 2-bromohexane from *n*-hexyl bromide?

3. Two grams of a mixture of butyraldehyde and ethyl ketone produced 5.4 g of silver metal when treated with excess Tollens' reagent. What was the percentage of butyraldehyde in the mixture?

4. Write balanced equations for (a) the oxidation of hexanal to hexanoic acid ($C_5H_{11}COOH$) with potassium permanganate in alkaline solution and (b) the oxidation of 2-hexanol to 2-hexanone with potassium dichromate in acid solution.

5. An unknown compound of carbon, hydrogen, and oxygen contains 69.77% carbon and 11.63% hydrogen, and has a molecular weight of 86. It does not reduce Fehling's solution, but forms a bisulfite addition compound and gives a positive iodoform test. What is a possible structure of the unknown compound?

6. A compound Y containing C, H, and O was subjected to quantitative analysis. A sample weighing 0.195 g gave 0.429 g CO_2 and 0.234 g H_2O. When 10 g of Y was treated with sodium metal, 1867 ml of H_2 (STP) were liberated. The compound Y is neutral to litmus paper and is unaffected by Fehling's solution. Oxidation of Y by $\frac{1}{3}$ mole equivalent of $K_2Cr_2O_7$ gave a compound which reduced ammoniacal silver nitrate. What is the probable formula of Y?

7. How could one distinguish methyl from ethyl alcohol qualitatively?

8. Without using fractional distillation, other than the separation from ethyl ether or water, how would one separate and isolate the components in the following mixtures: (a) acetone, hexanal, and heptane; (b) 2,4-dimethyl-3-heptanone, heptanal, and ethylene glycol?

9. What weight of the phenylhydrazone could be produced from 17.2 g of 3-pentanone if the yield is 92%?

10. What weight of each organic substance would be required to make 17.2 g of α-methylbutyraldehyde, starting with 2-bromobutane and any desired chemicals?

11. A one-gram sample of crude butyraldehyde was treated with Fehling's solution and 0.716 g of cuprous oxide was precipitated. What was the per cent purity of the aldehyde?

12. What series of reactions would one use to convert *n*-butanal to (a) *sec*-butanol, (b) 2-butanone, (c) propionic acid, CH_3CH_2COOH?

13. What series of reactions could one use (a) to prepare 4-methyl-2-pentyne from isovaleraldehyde; (b) to convert 3-methyl-2-pentanone to α-methylbutyric acid, $CH_3CH_2CH(CH_3)COOH$?

14. Indicate the series of laboratory reactions one could use to transform *p*-$CH_3CH{=}CH{-}C_6H_4{-}CHO$ into *p*-$CH_3CH{=}CH{-}C_6H_4{-}COOH$.

15. What weight of CrO_3 is required to prepare *p*-bromobenzaldehyde from 17.1 g of *p*-bromotoluene if a 10% excess of the oxidizing agent is to be used?

$$Cr = 52; \quad Br = 80$$

16. Explain the fact that a certain substance is stable in air, but when mixed with benzaldehyde it is oxidized in air?

17. How could one separate and isolate the components from the following mixtures without using fractional distillation other than the separation from ether?

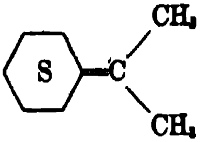
(a) Benzaldehyde, nitrobenzene, and benzoic acid.
(b) Salicylaldehyde, *p*-nitrophenol, *p*-bromobenzaldehyde, *p*-tolyl ethyl ketone, and *N,N*-dimethylaniline.

18. What weight of MnO_2 would be required to oxidize 92 g of toluene to benzaldehyde in sulfuric acid if the MnO_2 is only 97% pure? Mn = 55.

19. Using the aldol condensation as a first step, indicate the series of laboratory reactions you would use to prepare the following: (a) 1-butanol; (b) cinnamaldehyde, ϕ-CH=CH—CHO; (c) 2-formylcyclopentanol; (d) 2-propenylcyclohexene; (e) crotonaldehyde, CH_3—CH=CH—CHO; (f) pentaerythritol, $C(CH_2OH)_4$; (g) 4-methyl-2-pentanol; (h) C_6H_5—$C(OC_2H_5)_2$—CH=CH—CH_3.

20. Which should have the higher enol content, 2,4-hexanedione or 2,5-hexanedione? On what basis do you give your answer?

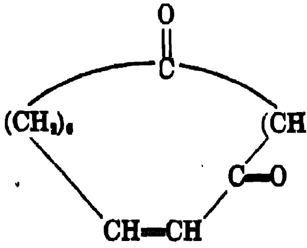
21. What series of reactions would you use to convert cyclohexanone into



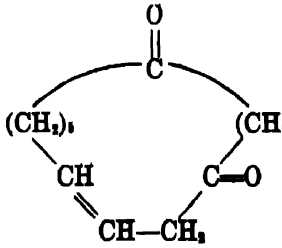
22. Offer an explanation for the fact that cyclopropanone exists as the hydrate in water solution.

23. The infrared $\nu_{C=O}$ and ν_{O-H} frequencies for benzoylacetone, $C_6H_5COCH_2COCH_3$, are 1603 and 2640 cm^{-1}, respectively. How do you account for such low values?

24. In the dehydrobromination of 2-bromo-1,10-cycloheptadecadione, I, two unsaturated diketones A and B were isolated. Product A, a light yellow oil, had the following spectral properties. UV: λ_m = 227 mμ; ε 13,800; IR: ν = 1714, 1670, 1624, 987 cm^{-1}; n.m.r.: τ a doublet and a sextet in the vinyl proton range. Product B, a colorless oil, had the following spectral properties. UV: no selective absorption down to 200 mμ; IR: ν = 1718, 971 cm^{-1}. Assign structures to A and B from II and III and account for the spectral data in terms of the assigned structures.

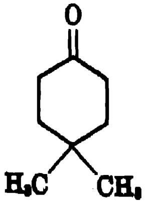


II



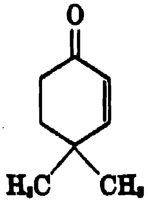
III

25. Assign the following spectroscopic data to the structural features of each compound responsible for the specific values:



R

ν = 1720 cm^{-1}

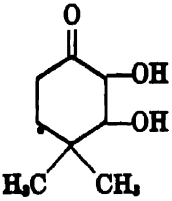


S

ν = 1680 cm^{-1}

λ_m = 224 mμ

ε 16,000

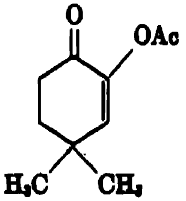


T

ν = 3570 cm^{-1}

3470

1715



V

ν = 1770 cm^{-1}

1700

1655

26. Divinyl carbinol was treated with MnO_2 in dry $CHCl_3$ in an air-free atmosphere, and the mixture was fractionally distilled in the presence of a trace of hydroquinone to give a fraction A with the following properties: Anal.: C, 73.10; H, 7.39. Fraction A gives a 2,4-dinitrophenylhydrazone. IR: 3050, 1672, 1620 cm^{-1}. Propose a structure for A based on the above information.

27. Offer an explanation for the observation that cyclohexanone readily forms a sodium bisulfite addition compound whereas diethyl ketone does not.

28. (See Section 21.1 for functional group absorption bands.) A compound S, C_4H_6O, has IR absorption bands at 1630, 1680, 2935, and 3075 cm^{-1}. Propose a structure for S on the basis of these data. Later, it was found that S forms a sodium bisulfite addition compound and reduces Tollens' reagent. Give a probable structure for S.

13

Carboxylic Acids

Monocarboxylic acids are those compounds with a single COOH group, usually designated by the formula R—COOH or ϕ—COOH. Inasmuch as several familiar members of the aliphatic series are obtained from fats, the RCOOH compounds are referred to as the fatty acids.

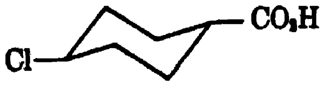
13.1 NOMENCLATURE

The I.U.C. system of naming the aliphatic carboxylic acids replaces the *-e* of *-ane* with *-oic*. For example, the first five acids have the names methanoic, ethanoic, propanoic, butanoic, and pentanoic acids. Again, the numbering starts with the carboxyl carbon atom. On the other hand, many of the acids have trivial names in which the carbon atoms are designated according to the Greek alphabet, beginning with the carbon atom *adjacent* to the carboxyl group. Several illustrations are given for both systems in Table 13.1.

TABLE 13.1. ALIPHATIC CARBOXYLIC ACID NOMENCLATURE

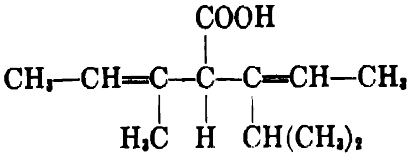
(The word *acid* has been omitted in all cases for brevity)

Structure	I.U.C. Name	Common Name
$H—COOH$	Methanoic	Formic
$CCl_3—COOH$	Trichloroethanoic	Trichloroacetic
$CH_3—CHBr—COOH$	2-Bromopropanoic	α-Bromopropionic
$CH_3CH_2CH_2COOH$	Butanoic	*n*-Butyric
$CH_3—CH(CH_3)—COOH$	2-Methylpropanoic	α-Methylpropionic or isobutyric
$CH_3CH_2CH_2CH_2COOH$	Pentanoic	Valeric
$CH_3—CH═CH—COOH$	2-Butenoic	Crotonic
$CH_3(CH_2)_4COOH$	Hexanoic	Caproic
$CH_3(CH_2)_6COOH$	Octanoic	Caprylic
$CH_3(CH_2)_8COOH$	Decanoic	Capric
$CH_3(CH_2)_{10}COOH$	Dodecanoic	Lauric
$CH_3(CH_2)_{12}COOH$	Tetradecanoic	Myristic
$CH_3(CH_2)_{14}COOH$	Hexadecanoic	Palmitic
$CH_3(CH_2)_{16}COOH$	Octadecanoic	Stearic



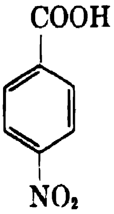
4-Chlorocyclohexane carboxylic acid

As with the aldehydes and ketones, it is sometimes simpler to regard the carboxyl group as a substituent, in which case it is called *carboxyl.* For illustration,

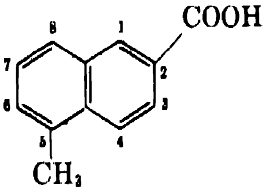


$$\begin{array}{c} COOH \\ | \\ CH_3-CH=\underset{\displaystyle H_3C}{\underset{|}{C}}-\underset{\displaystyle H}{\underset{|}{C}}-\underset{\displaystyle CH(CH_3)_2}{\underset{|}{C}}=CH-CH_3 \end{array}$$

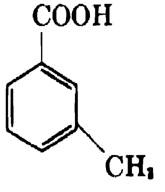
could be named 3-isopropyl-4-carboxyl-5-methyl-2,5-heptadiene. The aromatic acids are named as derivatives of the parent acid, which usually has a trival name. Several examples are given below for illustration.



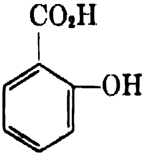
p-Nitrobenzoic acid



5-Methyl-2-naphthoic acid



m-Toluic acid



Salicylic acid

13.2 PREPARATION OF MONOCARBOXYLIC ACIDS

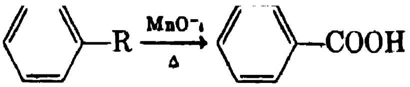
Again, unless otherwise indicated, the reactions taken up here apply to aliphatic and aromatic systems.

a. Oxidation of primary alcohols or aldehydes. It will be recalled that the successive oxidation stages of primary alcohols are alcohol, aldehyde, acid.

$$R-CH_2OH \xrightarrow{\text{oxid.}} R-CHO \xrightarrow{\text{oxid.}} R-COOH$$

Although aldehydes are at a higher oxidation level than alcohols, they are more easily oxidized than alcohols, so that ease of oxidation is not directly related to oxidation level. Acids are extremely hard to oxidize and are inert to all but extremely powerful oxidizing agents. Therefore, the usual chemical oxidizing agents, such as potassium dichromate or permanganate, will serve to oxidize primary alcohols or aldehydes to carboxylic acids in good yields. Of course, the oxidation of ketones, unsaturated hydrocarbons, and other types of compounds will yield acids, too, but usually mixed or unpredictable products are obtained. For this reason attention is focused upon the oxidation of primary alcohols or aldehydes where the carbon skeleton remains the same during oxidation.

It was pointed out in Section 8.2 that vigorous oxidation of any carbon-attached side-chain to an aromatic ring converts the group into a COOH group.



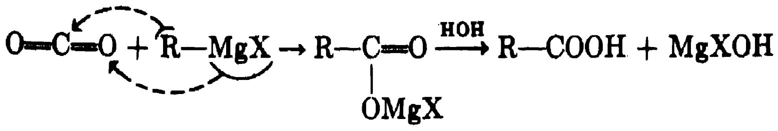
Normally, alkaline permanganate, acid dichromate, or dilute nitric acid is used as the oxidant.

b. Hydrolysis of alkyl cyanides. Except in rare cases, hydrolyses are always catalyzed by acid or base. In most cases, one or the other is to be preferred, and sometimes only one will work, as in the acid hydrolysis of ethers or acetals. Organic cyanides (see Section 16.3c), also called *nitriles*, can be hydrolyzed in acid or base.

$$R—CN + 2H_2O \xrightarrow{H_3O^+ \text{ or } OH^-} R—COOH + NH_3$$

It is to be realized that acid hydrolysis yields the organic acid and an ammonium salt ($RCOOH + NH_4^+$), whereas basic hydrolysis yields the salt of the organic acid plus ammonia ($RCO_2^- + NH_3$).

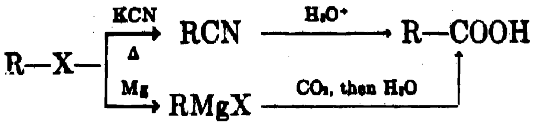
c. Carbonation of a Grignard. In typical fashion, Grignard reagents add to carbon dioxide as they do to other C═O bonds.



$$O{=}C{=}O + R—MgX \rightarrow R—\underset{\displaystyle OMgX}{\underset{|}{C}}{=}O \xrightarrow{HOH} R—COOH + MgXOH$$

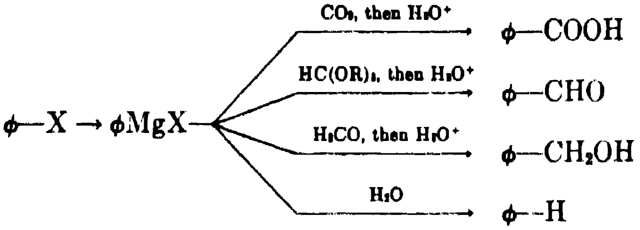
The addition product is easily hydrolyzed to the acid, and the two successive steps are carried out in the same reaction vessel.

These latter two methods of preparing carboxylic acids provide routes for changing an alkyl halide to a carboxylic acid, i.e., for replacing X in R—X by COOH.



Both routes give good yields in general, and the selection of either is usually based upon the nature of R. That is, if R has a group present that would react with a Grignard, for example OH, then the nitrile route would be chosen.

The use of Grignards for replacing a halogen atom by several important groups can now be summarized as follows:



c. Hydrolysis of benzotrichlorides. One more useful preparative reaction in the aromatic series is the hydrolysis of benzotrichlorides:

$$\phi\text{—}CCl_3 + 2H_2O \xrightarrow{H_3O^+} \phi\text{—}COOH + 3HCl$$

The benzotrichlorides can be prepared by side-chain chlorination of the respective toluenes. Therefore, either by oxidation or side-chain halogenation and subsequent hydrolysis, substituted toluenes may be converted into the respective benzoic acids. The hydrolysis can be catalyzed by either acid or base.

The commercial production of monocarboxylic acids is generally through the oxidation of the corresponding alcohols or aldehydes with air in the presence of catalysts such as vanadium or cerium oxides.

13.3 PHYSICAL PROPERTIES

Carboxylic acids form relatively strong hydrogen bonds, which fact is reflected in their physical properties. For example, they have high boiling points for their respective molecular weights, higher even than the corresponding methyl or ethyl esters.

COMPARISON OF BOILING POINTS OF ACIDS AND ESTERS

	Acid	*Ethyl Ester*
HCOOH	101°	54°
CH_3COOH	118	77
C_2H_5COOH	141	99

TABLE 13.2. PHYSICAL CONSTANTS OF SOME CARBOXYLIC ACIDS

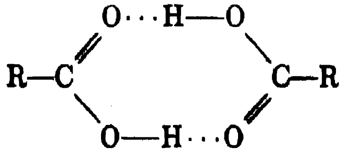
Name	Melting Point	Boiling Point	pK_a
Formic	8.4	101	3.77
Acetic	16.6	118	4.76
Propionic	−22	141	4.88
n-Butyric	−4.7	163	4.82
n-Valeric	−35	187	4.81
Phenylacetic	77	266	4.31
Acrylic	13	141	4.26
Benzoic	122	249	4.17
p-Toluic	180	275	4.35
p-Nitrobenzoic	240		3.40
Salicylic	159		3.00
p-Hydroxybenzoic	215		4.54
Anisic	184		4.49

As noted in Section 10.5, hydrogen bonding with water leads to greater solubilities, and the first four acids are miscible with water. In contrast to this, their esters have much smaller solubilities. See Table 13.3.

TABLE 13.3. PERCENTAGES OF WATER SOLUBILITY NEAR ROOM TEMPERATURE OF SOME ACIDS AND THEIR ETHYL ESTERS

	Acid	*Ethyl Ester*
HCOOH	∞	11
CH_3COOH	∞	8.5
C_2H_5COOH	∞	2.4
C_3H_7COOH	∞	0.7
$C_5H_{11}COOH$	3.3	Insoluble

The hydrocarbon portion of the acids resists entering into water solution, and when it becomes large, this resistance outweighs the solubilizing effect of hydrogen bonding. This occurs in the case of valeric and higher acids and the aromatic acids in general. It is to be noted that carboxylic acids tend to form dimers rather than polymeric chain aggregates as alcohols do.



A dimeric carboxylic acid

The degree of association decreases with rising temperature because as the temperature is raised, the kinetic energy of the molecules increases and eventually breaks the hydrogen bonds to form monomeric molecules.

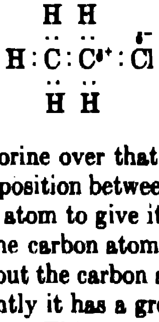
The most typical property of carboxylic acids is their acidic character. They are the common organic acids. However, in contrast to mineral acids, such as hydrochloric and sulfuric acids, carboxylic acids are relatively weak acids. Their dissociation in aqueous solution can be expressed by the usual law of mass action,

$$H_2O + RCOOH \rightleftharpoons RCO_2^- + H_3O^+$$

$$K_a = \frac{(RCO_2^-)(H_3O^+)}{(RCO_2H)(H_2O)} \simeq 10^{-5}$$

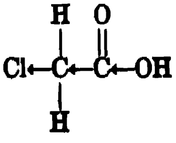
where the quantities in parentheses represent concentrations. For simple acids, K_a is of the order of magnitude of 10^{-5}, and a 1 M aqueous solution of such an acid would have a pH near 3. However, certain structural features may increase the acid strength of carboxylic acids ten-thousandfold. For example, the perfluorocarboxylic acids, $C_nF_{2n-1}COOH$, are strong acids, and aqueous solutions have essentially the same pH as would be calculated for complete dissociation.

This acid strengthening effect of fluorine is due to *induction*. It can be explained as follows: in a neutral covalent molecule such as that of chloroethane,



$$\begin{array}{cccc} & \text{H} & \text{H} & \\ \text{H}: & \ddot{\text{C}}: & \ddot{\text{C}}^{\delta+}: & \overset{\delta-}{\text{Cl}} \\ & \ddot{\text{H}} & \ddot{\text{H}} & \end{array}$$

the greater electronegativity of chlorine over that of carbon attracts the shared pair of electrons away from the midway position between the two atoms. This increases the electron density about the chlorine atom to give it a partial negative charge, and decreases the electron density about the carbon atom to give it a partial positive charge. The decrease in electron density about the carbon atom causes it to have an increased affinity for electrons, and consequently it has a greater attraction for electrons (electronegativity) than the β-carbon atom. This brings about a small displacement of the electrons in the C—C bond toward the α-carbon atom, which, in turn, decreases the electron density about the β-carbon atom to produce there a fractional positive charge. This situation can be described, in different words, by saying that the chlorine atom induces a positive charge on the α-carbon atom, which, in turn, induces a smaller positive charge on the β-carbon atom. In this fashion Lewis first explained the acid strengths of the chloroacetic acids.



$$\begin{array}{ccccccc} & & \text{H} & & \text{O} & & \\ & & | & & \| & & \\ \text{Cl} & \leftarrow & \text{C} & \leftarrow & \text{C} & \leftarrow & \text{OH} \\ & & | & & & & \\ & & \text{H} & & & & \end{array}$$

In chloroacetic acid, the chlorine atom pulls the electron pair toward itself and thereby induces a positive charge on the α-carbon atom; in turn, progressively smaller positive charges are induced on the carboxyl-carbon atom and the hydroxyl-oxygen atom. The hydroxyl-oxygen atom of chloroacetic acid is, therefore, more positive than that of unsubstituted acetic acid, and this facilitates dissociation of the proton. As a result, chloroacetic acid is a stronger acid than is acetic acid. Moreover, the more chlorine atoms there are on the α-carbon atom, the greater will be the induced positive charge on the hydroxyl-oxygen atom. Accordingly, dichloroacetic acid should be stronger than monochloroacetic acid, and the trichloro acid should be still stronger. This is actually the case, with trichloroacetic acid being a strong acid. The same sequence is found for the fluoroacetic acids.

Dissociation Constants ($\times 10^3$) *of Some Halogen Acetic Acids*

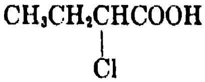
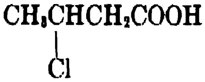
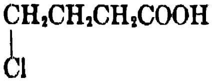
X	XCH_2COOH	$X_2CHCOOH$	X_3CCOOH
Cl	1.4	50	130
F	2.2	57	500

Since the hydrogen atom is more electronegative than an alkyl group, formic acid is a stronger acid than the simple aliphatic acids.

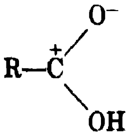
$$HCOOH \quad K_a = 1.77 \times 10^{-4}$$

$$CH_3COOH \quad K_a = 1.75 \times 10^{-5}$$

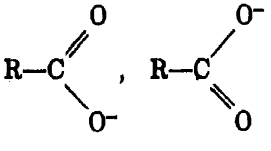
The transmission of induced charges along a chain of bonded atoms is called *chain induction*. The effect decreases rapidly with distance, as shown by the order of decreasing acid strengths of α-, β-, and γ-chlorobutyric acids, where the chlorine atom is progressively moved away from the carboxyl group.

	$K_a \times 10^5$
 $CH_3CH_2CH(Cl)COOH$	139
 $CH_3CH(Cl)CH_2COOH$	8.9
 $ClCH_2CH_2CH_2COOH$	3

The fact that carboxylic acids as a class are stronger acids than alcohols is explained in terms of *induction* and *resonance*. Owing to the ionic character of the carbonyl group,



the carbon atom has a larger electronegativity than does an alcohol carbon atom. It therefore induces a partial positive charge on the hydroxyl-oxygen atom of the acid which facilitates the escape of the proton. Also, the carboxylate ion is stabilized by resonance to a greater extent than is the acid form, owing to the exact equivalence of the two structures,



and this shifts the equilibrium in the direction of ionization. Such resonance stabilization does not occur for the ion of an alcohol.

Benzoic acids have dissociation constants of the same order of magnitude as fatty acids, $K_a \simeq 10^{-5}$. They dissolve, ther fore, in dilute aqueous sodium carbonate or bicarbonate (Section A-5); however, if one wanted to make a solution of the salt, aqueous sodium hydroxide would be more effective. Most aromatic acids are white, crystalline solids, and easily recrystallized from aqueous alcohol. Aromatic acids are not volatile in steam, although benzoic acid is exceptional in this respect. The COOH group is *m*-orienting and ring-deactivating, but not to the extent of a NO_2 group.

13.4 CHEMICAL PROPERTIES

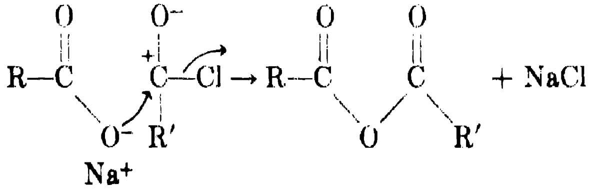
The carboxyl group is made up of a carbonyl and a hydroxyl group, but the typical properties of these two classes of compounds, aldehydes and alcohols. are somewhat altered in the acid. For example, carboxylic acids do not undergo the addition reactions typical of aldehydes, and the acids are stronger acids than alcohols (alcohols are neutral in aqueous media). Thus, the proximity of the two groups making up the carboxyl group brings about an alteration in their typical properties, but the change is more pronounced for the carbonyl group. It will be observed that the acids undergo many of the reactions typical of alcohols, but few in common with aldehydes and ketones.

a. Salt formation. As is to be expected, carboxylic acids form salts with strong bases:-

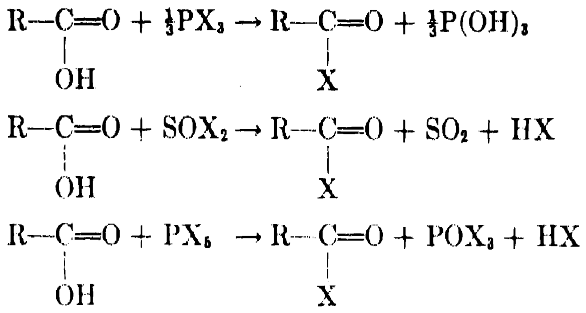
$$R{-}COOH + NaOH \rightarrow R{-}COONa + HOH$$

Salt formation with bases significantly weaker than ammonia will be slight because of the weakness of carboxylic acids. Most sodium and potassium salts are water soluble; hence, fatty acids generally dissolve in dilute alkali.

b. Anhydride formation. The hydroxyl-hydrogen atom of carboxylic acids is replaceable by acyl groups, but the reaction is carried out by using the salt.



c. Acid halide formation. The OH group of acids may be replaced by halogens with the same reagents as used with alcohols except HX acids.



$$\mathrm{R{-}\underset{\underset{OH}{|}}{C}{=}O + \tfrac{1}{3}PX_3 \rightarrow R{-}\underset{\underset{X}{|}}{C}{=}O + \tfrac{1}{3}P(OH)_3}$$

$$\mathrm{R{-}\underset{\underset{OH}{|}}{C}{=}O + SOX_2 \rightarrow R{-}\underset{\underset{X}{|}}{C}{=}O + SO_2 + HX}$$

$$\mathrm{R{-}\underset{\underset{OH}{|}}{C}{=}O + PX_5 \rightarrow R{-}\underset{\underset{X}{|}}{C}{=}O + POX_3 + HX}$$

d. Ester formation. $RCOOH + R'OH \rightleftharpoons RCOOR' + HOH$. The esterification of alcohols was discussed in Section 10.6c and need not be taken up here. More will be said about the reaction and about these last three classes of compounds (anhydrides, acid halides, and esters) when each class is taken up as a family.

e. Oxidation and reduction. With the exception of formic acid, the saturated carboxylic acids are reasonably inert to oxidation by common chemical oxidizing agents such as potassium dichromate and permanganate. However, fatty acids can be oxidized by hydrogen peroxide with iron salt catalysts to give acids of two fewer carbon atoms.

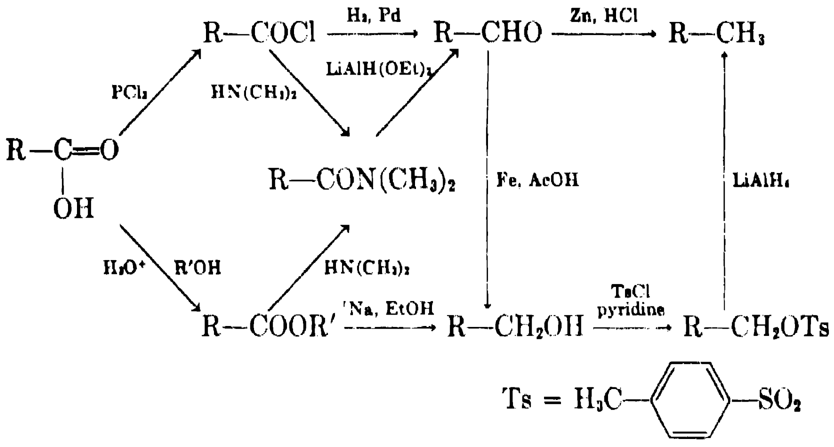
$$C_nH_{2n+1}CH_2CH_2COOH \xrightarrow{H_2O_2,\ Fe^{++}} C_nH_{2n+1}COOH + 2CO_2 + 2H_2O$$

The biochemical degradation of fatty acids in cells, important as a means of getting heat and energy from the fats in our diet, also takes place by two carbon-atom cleavages (Section 15.7c). Hence, acids containing an even number of carbon atoms are broken down to acetic acid. The odd-numbered members are not normally found in biological systems. In connection with this, it is interesting that ω-fluorocarboxylic acids, $FCH_2{-}(CH_2)_n{-}COOH$, with an even number of carbon atoms would end up as the toxic FCH_2COOH from biochemical degradation, and the odd-numbered acids would yield the nontoxic FCH_2CH_2COOH. Similarly, esters of the ω-fluoroacids with an even number of carbon atoms are toxic, whereas the esters of the odd-numbered acids produce no ill effects.

Prior to the appearance of the mixed metal hydrides (see page 488 ff) just after World War II, the laboratory reduction of acids was impractical. Now they can be easily reduced to the corresponding alcohols with $LiAlH_4$ or $NaBH_4$.

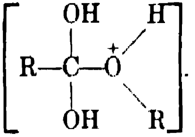
$$\begin{array}{c} 4RCOOH + 3LiAlH_4 \rightarrow \underbrace{(RCH_2O)_3Al + RCH_2OLi} + 2LiAlO_2 + 4H_2 \\ \Big\downarrow{\scriptstyle H_2O} \\ 4RCH_2OH + Al(OH)_3 + LiOH \end{array}$$

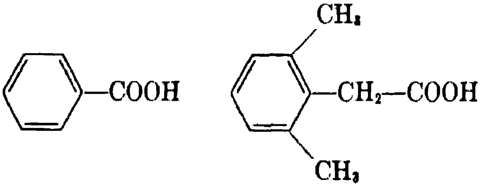
Formerly acids were reduced indirectly by converting them into esters or acid chlorides for reduction to alcohols or aldehydes, respectively.



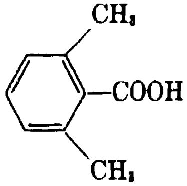
Generally the reduction of an acid to an aldehyde is done indirectly through the acid chloride, although a carboxylic acid can be reduced directly to the aldehyde with lithium metal in ethylamine. The yields are too variable for the latter reaction to serve as a dependable general method.

Aromatic acids have essentially all of those properties of fatty acids which are due to the presence of the COOH group. Hence, both types form salts, esters, acid chlorides, anhydrides, and amides.

According to the mechanism given for esterification in Section 15.2, the path for esterification is just the reverse for the hydrolysis of esters. This is the normal, mild acid-catalyzed method. It depends on the formation of a tetrahedral transition state  . For those acids and esters with large groups attached to R, such as in trimethylacetic and 2,6-dimethylbenzoic acids, there is a steric hindrance to the formation of this intermediate, and reaction is either very slow or does not occur. For example, trimethylacetic acid is very slowly esterified, and 2,6-dimethylbenzoic and 2,6-dimethylcyclohexane carboxylic acids are unreactive. However, if the 2,6-dimethylphenyl group is moved back from the COOH group, as in 2,6-dimethylphenylacetic acid, then normal esterification will take place.

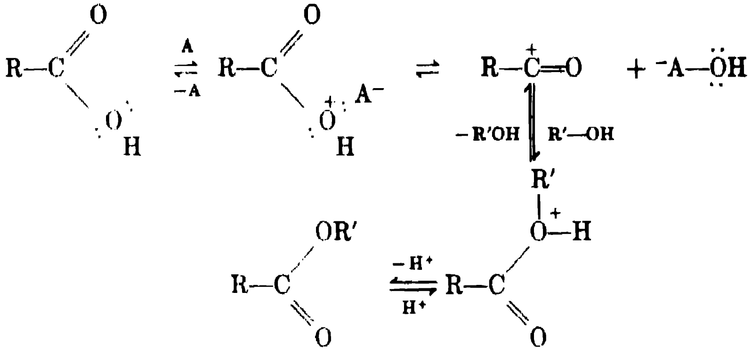


Offer no steric hindrance to esterification



Offers steric hindrance to esterification

On the other hand, esterification proceeds by a different mechanism in strong acid media, such as in concentrated sulfuric acid or trifluoroacetic anhydride, and only hindered acids or esters tend to react in these strong acid solutions. A is a Lewis acid.



It takes a strong acid to form the acyl carbonium ion, and, owing to a lack of steric hindrance in this ion, it can form in the case of hindered acids or esters.

Just as with the aliphatic acids, reduction of the COOH group to the CHO group has to be done by first converting the COOH group to some other group, such as the acid chloride, hydrazide, or cyanide.

There is one type of carboxylic acid which can be reduced directly to the aldehyde. Substituted salicylic acids can be reduced with sodium amalgam in an aqueous boric acid-toluidine mixture. As the aldehyde is formed, it condenses to form a Schiff base. Only *o*-hydroxybenzoic acids are reducible by this method.

f. Degradations of carboxylic acids. Carboxylic acids and their salts undergo decarboxylation to produce various classes of compounds. The influence of the type of salt upon the course of the reaction can be noted.

(1) *To alkyl halides:*

$$RCOOAg + X_2 \xrightarrow[\Delta]{CCl_4} R{-}X + CO_2 + AgX$$

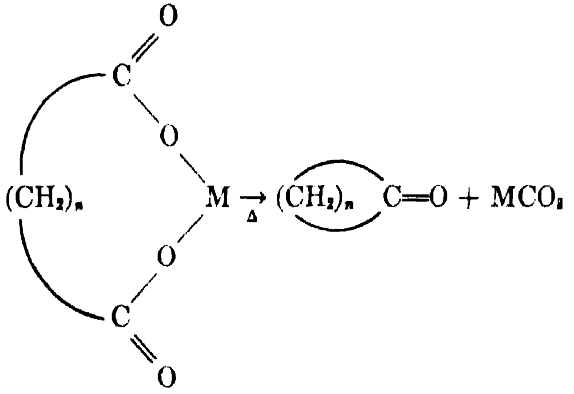
This reaction, the *Hunsdiecker reaction*, is very useful because the resulting alkyl or aryl halides are often key substances in multistep syntheses. The silver salts may be formed by neutralizing the carboxylic acids with ammonia and precipitating the silver salts by the addition of aqueous silver nitrate. Often chloro compounds are produced as side-products when bromine is used. This can be avoided by using 1,2-dibromoethane as the solvent in place of the CCl_4. Mercuric oxide can be used for this reaction in place of silver, in which case the acid can be used directly without prior isolation of the salt.

(2) *To amines:*

$$RCOOH + HN_3 \rightarrow RNH_2 + CO_2 + N_2$$

Hydrazoic acid, HN_3, is not to be confused with ammonia, H_3N. The acid is very unstable and not kept in stock. Instead, sodium azide, which is stable, is used with sulfuric acid. A common procedure is to dissolve the carboxylic acid in concentrated sulfuric acid, cover with chloroform, and then add sodium azide in portions. The reaction, known as the *Schmidt reaction*, is useful for going from a carboxylic acid to an amine as a step in multistep syntheses.

(3) *To a ketone:*



We saw in Section 5.2 that this reaction can be used to prepare certain ring-size alicyclic ketones. It is not a general preparative method for aliphatic ketones, although some ketones are produced commercially by passing the vapors of fatty acids over catalytic amounts of MnO_2. When a mixture of an aromatic acid and an aliphatic acid is heated with iron metal at 250–300°, a fairly good yield of the respective phenone is sometimes obtained.

$$\phi CO_2H + RCO_2H + Fe \xrightarrow[\Delta]{280^\circ} \phi—CO—R + FeO + CO_2 + H_2$$

Little R_2CO or ϕ_2CO is produced. The reaction offers a means of making meta substituted phenones which cannot be obtained by acylations through a Friedel-Crafts reaction, e.g., *m*—Cl—C_6H_4—COR.

(4) *To an amide:*

$$R—CO_2NH_4 \xrightarrow[\Delta]{250^\circ} R—CONH_2 + H_2O$$

This, of course, is not a degradation. It is included as a pyrolysis of a salt of a carboxylic acid.

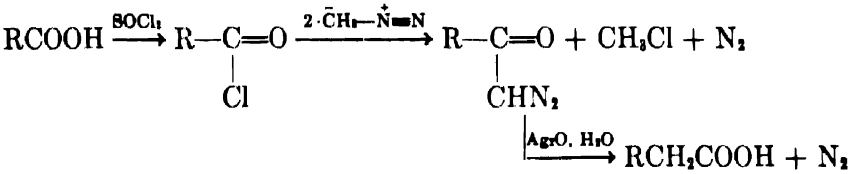
(5) *Replacement by H:*

When COOH groups are attached to electronegative carbons, CO_2 is lost fairly easily:

$$\phi—COOH \xrightarrow[CaO,\ \Delta]{2NaOH} \phi—H + Na_2CO_3$$

Other important examples will be taken up in the sections on dicarboxylic acids and esters.

g. Next higher homolog formation. As a method of converting acids to the next higher homologs, the *Arndt-Eistert synthesis* consists of the following sequence of reactions:

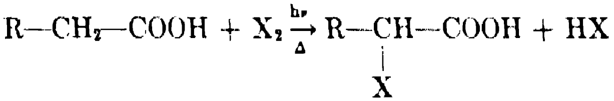


$$\mathrm{RCOOH} \xrightarrow{\mathrm{SOCl_2}} \underset{\substack{|\\ \mathrm{Cl}}}{\mathrm{R{-}C{=}O}} \xrightarrow{2\cdot\bar{\mathrm{C}}\mathrm{H_2{-}}\overset{+}{\mathrm{N}}{\equiv}\mathrm{N}} \underset{\substack{|\\ \mathrm{CHN_2}}}{\mathrm{R{-}C{=}O}} + \mathrm{CH_3Cl} + \mathrm{N_2}$$

$$\xrightarrow{\mathrm{Ag_2O,\ H_2O}} \mathrm{RCH_2COOH} + \mathrm{N_2}$$

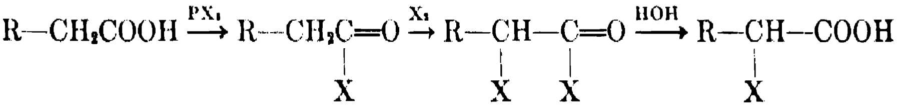
Diazomethane, CH_2N_2, is an unstable compound which is prepared and used in ether solution. The acid chloride is added to an excess of diazomethane yielding the diazoketone, which decomposes in the presence of moist silver oxide to give the acid. (See also page 364.)

h. Side-chain halogenation. Although carboxylic acids are difficult to halogenate, halogenation at the α-carbon atoms may be carried out. Two catalytic techniques are employed, either illumination plus heat or phosphorus trihalide.



$$\mathrm{R{-}CH_2{-}COOH} + \mathrm{X_2} \xrightarrow[\Delta]{h\nu} \underset{\substack{|\\ \mathrm{X}}}{\mathrm{R{-}CH}}\mathrm{{-}COOH} + \mathrm{HX}$$

When PX_3 is used, the reaction is known as the *Hell-Volhard-Zelinsky reaction*. The acid is transformed into the acid halide, the latter then undergoes halogenation, and the α-halogen acid is produced through hydrolysis.



$$\mathrm{R{-}CH_2COOH} \xrightarrow{\mathrm{PX_3}} \mathrm{R{-}CH_2}\underset{\substack{|\\ \mathrm{X}}}{\mathrm{C}}\mathrm{{=}O} \xrightarrow{\mathrm{X_2}} \mathrm{R{-}}\underset{\substack{|\\ \mathrm{X}}}{\mathrm{CH}}\mathrm{{-}}\underset{\substack{|\\ \mathrm{X}}}{\mathrm{C}}\mathrm{{=}O} \xrightarrow{\mathrm{HOH}} \mathrm{R{-}}\underset{\substack{|\\ \mathrm{X}}}{\mathrm{CH}}\mathrm{{-}COOH}$$

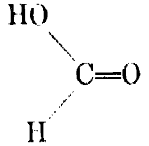
In the presence of peroxides, fatty acids may be halogenated just as are alkanes (see Section 2.7). In this case, halogenation may occur any place along the chain. For example, the peroxide catalyzed chlorination of *n*-butyric acid yields 10 per cent α-, 45 per cent β-, and 45 per cent γ-chlorobutyric acids.

13.5 SOME INDIVIDUAL ACIDS

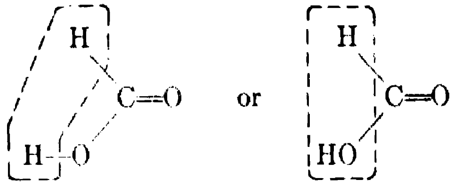
Formic acid (L. *formica*, ant) occurs in the free state in the red ant, from which it may be isolated by crushing and steam distillation. When concentrated, it has a pungent odor and will blister the skin. It is produced commercially by the reaction of carbon monoxide with sodium hydroxide, followed by acidification.

$$\mathrm{CO} + \mathrm{NaOH} \xrightarrow[\text{8 atm.}]{200°} \mathrm{H{-}COONa} \xrightarrow{\mathrm{H_3O^+}} \mathrm{H{-}COOH}$$

Unlike the rest of the carboxylic acids, the structure of formic acid may be regarded as a hydroxylated aldehyde.



Thus it essentially is an aldehyde and actually has a certain resemblance to aldehydes. For instance, it reduces Tollens' reagent. Upon heating, formic acid decomposes in one of two ways:



$$2HCOOH \xrightarrow[\Delta]{} \underline{H_2 + CO_2} + \underline{H_2O + CO}$$

Certain agents, particularly metals, catalyze the decomposition to produce hydrogen plus carbon dioxide; other agents, notably dehydrating agents, lead to the formation of water plus carbon monoxide. As such, formic acid and sodium formate have served as laboratory sources of carbon monoxide by the addition of concentrated sulfuric acid.

Acetic acid (L. *acetum*, vinegar) is the most common of the organic acids. Its dilute aqueous solutions have been known since ancient times, because it is formed in alcoholic beverages upon exposure to air. It is the sour principle of vinegar, resulting from the enzymatic oxidation of the ethyl alcohol produced in fermentation. Cider, the usual source of vinegar, is allowed to drop slowly over beechwood shavings while air is forced upwards. Acetic acid was obtained formerly from the pyrolysis of wood (along with methyl alcohol and acetone) but now most of it is produced by the catalytic air oxidation of ethanol or by oxidation of the acetaldehyde produced in the hydration of acetylene. Pure acetic acid is called *glacial acetic acid*. Acetic acid is found as a common reagent in chemical laboratories, and in industry it is used for the synthesis of many compounds such as esters, perfumes, dyes, pharmaceuticals, and especially plastics.

Butyric acid (L. *butyrum*, butter) is present as the ester of glycerol in butter, and its odor is responsible for the unpleasant odor of rancid butter and stale perspiration. The long-chain fatty acids, such as stearic and palmitic, will be discussed along with the fats in Section 15.7.

13.6 DICARBOXYLIC ACIDS

The aliphatic dicarboxylic acids of major importance are those in which the carboxyl groups are at the ends of a chain of methylene groups,

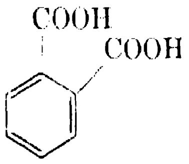
$HOOC—(CH_2)_n—COOH$. Thus they may be regarded as dicarboxyl derivatives of alkanes, called *alkanedioic acids*. The first five polymethylene dicarboxylic acids are named in Table 13.4.

TABLE 13.4. NAMES OF THE FIRST FIVE POLYMETHYLENE DICARBOXYLIC ACIDS

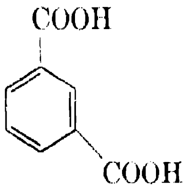
(For brevity, the word *acid* has been omitted from each name)

Structure	I.U.C. Name	Common Name*
$HOOC—COOH$	Ethanedioic	Oxalic
$HOOC—CH_2—COOH$	Propanedioic	Malonic
$HOOC—(CH_2)_2—COOH$	Butanedioic	Succinic
$HOOC—(CH_2)_3—COOH$	Pentanedioic	Glutaric
$HOOC—(CH_2)_4—COOH$	Hexanedioic	Adipic

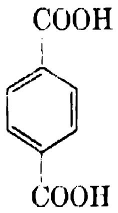
* Note that their initials correspond to those of the mnemonic, "Oh My Such Good Apples."



Phthalic acid

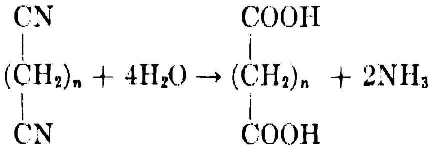


Isophthalic acid



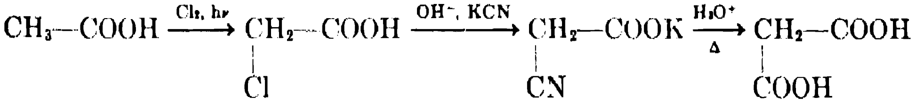
Terephthalic acid

Any of these acids may be prepared by hydrolysis of the corresponding dicyanides, beginning with cyanogen, $(CN)_2$.



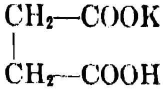
$$\begin{matrix} CN \\ | \\ (CH_2)_n \\ | \\ CN \end{matrix} + 4H_2O \rightarrow \begin{matrix} COOH \\ | \\ (CH_2)_n \\ | \\ COOH \end{matrix} + 2NH_3$$

Other methods of preparing these acids are given in Section 15.6. *Malonic acid* is also produced commercially from acetic acid by the sequence of reactions:



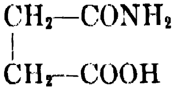
$$CH_3—COOH \xrightarrow{Cl_2,\ h\nu} \begin{matrix} CH_2—COOH \\ | \\ Cl \end{matrix} \xrightarrow{OH^-,\ KCN} \begin{matrix} CH_2—COOK \\ | \\ CN \end{matrix} \xrightarrow[\Delta]{H_3O^+} \begin{matrix} CH_2—COOH \\ | \\ COOH \end{matrix}$$

These dicarboxylic acids in general have properties characteristic of monocarboxylic acids. Thus, they form mono- or diesters, amides, acid halides, salts, etc.



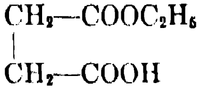
$$\begin{matrix} CH_2—COOK \\ | \\ CH_2—COOH \end{matrix}$$

Potassium acid succinate



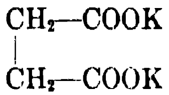
$$\begin{matrix} CH_2—CONH_2 \\ | \\ CH_2—COOH \end{matrix}$$

Succinamic acid



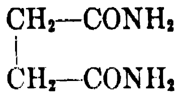
$$\begin{matrix} CH_2—COOC_2H_5 \\ | \\ CH_2—COOH \end{matrix}$$

Monoethyl succinate



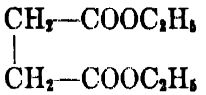
$$\begin{array}{l} CH_2{-}COOK \\ | \\ CH_2{-}COOK \end{array}$$

Potassium succinate



$$\begin{array}{l} CH_2{-}CONH_2 \\ | \\ CH_2{-}CONH_2 \end{array}$$

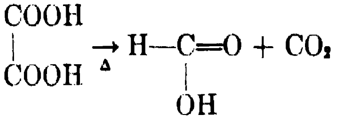
succinamide



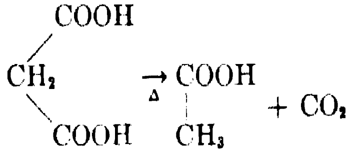
$$\begin{array}{l} CH_2{-}COOC_2H_5 \\ | \\ CH_2{-}COOC_2H_5 \end{array}$$

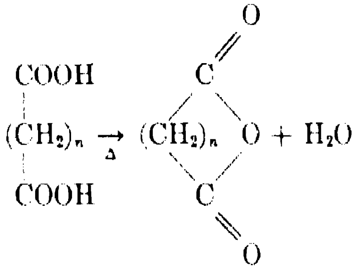
Diethyl succinate

Upon pyrolysis, the dicarboxylic acids lose carbon dioxide or water.

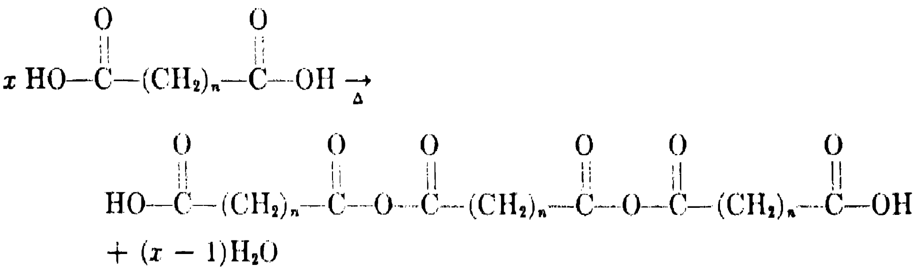


$$\begin{array}{l} COOH \\ | \\ COOH \end{array} \xrightarrow[\Delta]{} \begin{array}{l} H{-}C{=}O \\ \quad\ \ | \\ \quad\ \ OH \end{array} + CO_2$$





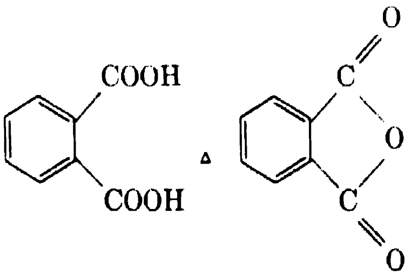
For $n = 2$ or 3, five- or six-membered-ring intramolecular anhydrides are produced. For n greater than 3, intermolecular polymeric anhydrides result.



$$x\,HO{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}(CH_2)_n{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}OH \xrightarrow[\Delta]{}$$

$$HO{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}(CH_2)_n{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}O{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}(CH_2)_n{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}O{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}(CH_2)_n{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}OH$$

$$+\ (x - 1)H_2O$$



Phthalic anhydride

Some of the dicarboxylic acids are used for making plastics (see Chapter 26). Phthalic acid is used extensively for making alkyd plastics (Section 26.3) and dyes (Section 27.3). Its dimethyl ester is used as a mosquito repellent, and the imide is used in Gabriel's synthesis of amines.

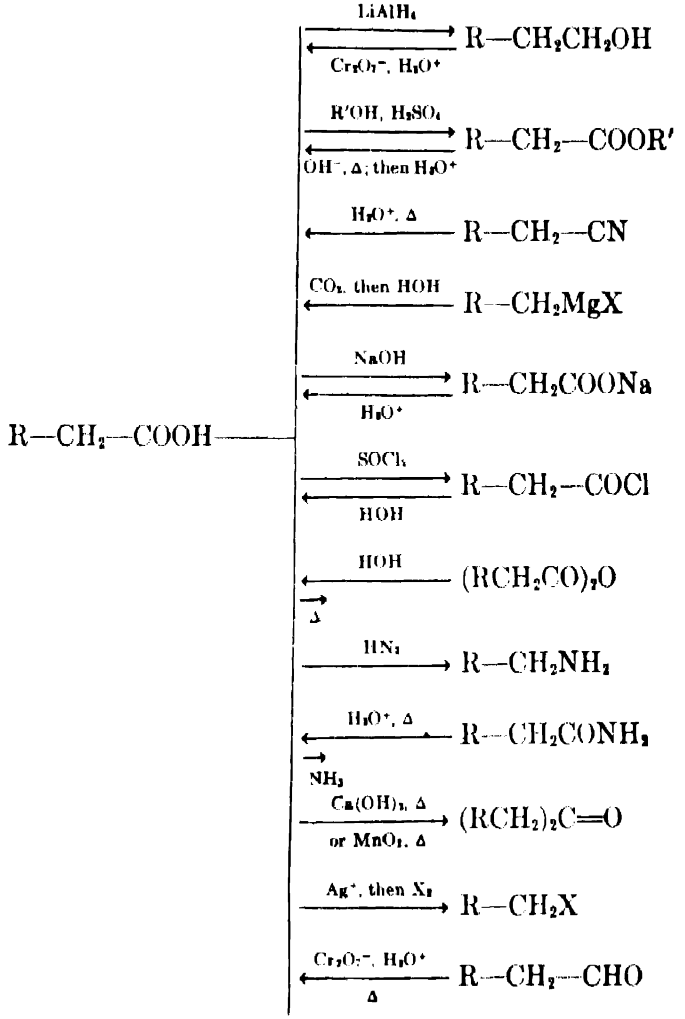
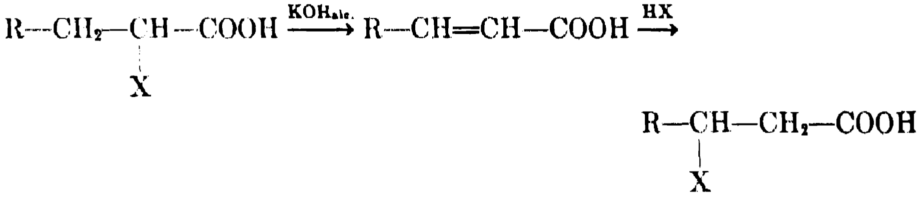


Fig. 13.1. Characteristic reaction chart for aliphatic monocarboxylic acids.

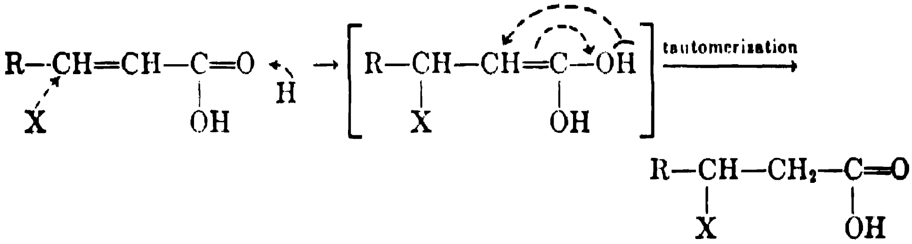
13.7 SUBSTITUTED CARBOXYLIC ACIDS

a. Halogenated acids. Like the alkyl halides, the side-chain halogenated acids are highly useful because they serve as convenient starting materials for preparing several other classes of compounds. The preparation of α-halogen acids, R—CHX—COOH, was described in Section 13.4h. β-Halogen acids are prepared from the *alpha* isomers by dehydrohalogenation and then hydrohalogenation.



$$R{-}CH_2{-}\underset{X}{\underset{|}{C}}H{-}COOH \xrightarrow{KOH_{alc.}} R{-}CH{=}CH{-}COOH \xrightarrow{HX} R{-}\underset{X}{\underset{|}{C}}H{-}CH_2{-}COOH$$

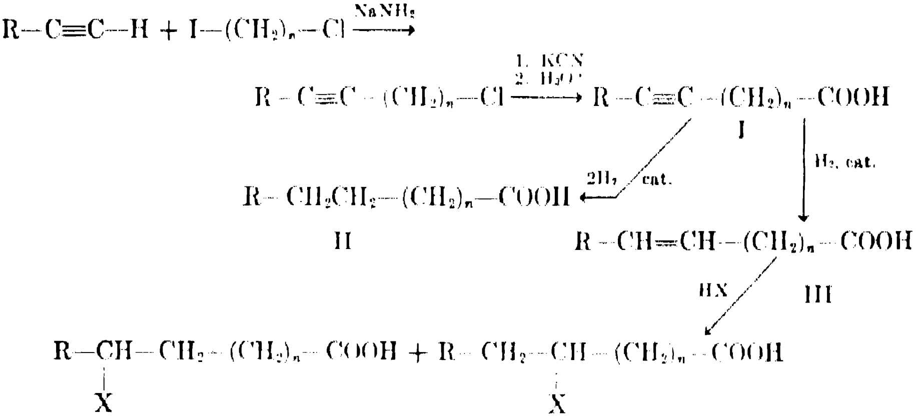
The addition of HX probably takes place by 1,4-addition and subsequent tautomerization.



$$R{-}\underset{X}{C}H{=}CH{-}\underset{OH}{\underset{|}{C}}{=}O + \underset{H}{} \rightarrow \left[R{-}\underset{X}{\underset{|}{C}}H{-}CH{=}\underset{OH}{\underset{|}{C}}{-}OH\right] \xrightarrow{\text{tautomerization}} R{-}\underset{X}{\underset{|}{C}}H{-}CH_2{-}\underset{OH}{\underset{|}{C}}{=}O$$

Since the electronegative halogen atom does not have a tendency to add to the electronegative oxygen atom, addition takes place only in the manner shown, producing only one product. When the double bond is in any other position of the side chain, this selective addition does not occur, and mixed products are obtained.

Other halogenated acids, as well as unsaturated acids, may be produced through a series of reactions as follows:



$$R{-}C{\equiv}C{-}H + I{-}(CH_2)_n{-}Cl \xrightarrow{NaNH_2} R{-}C{\equiv}C{-}(CH_2)_n{-}Cl \xrightarrow[2.\ H_2O]{1.\ KCN} \underset{\text{I}}{R{-}C{\equiv}C{-}(CH_2)_n{-}COOH}$$

$$\text{I} \xrightarrow{2H_2,\ cat.} \underset{\text{II}}{R{-}CH_2CH_2{-}(CH_2)_n{-}COOH}$$

$$\text{I} \xrightarrow{H_2,\ cat.} \underset{\text{III}}{R{-}CH{=}CH{-}(CH_2)_n{-}COOH}$$

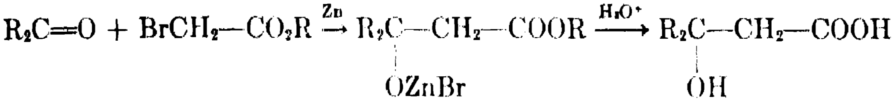
$$\text{III} \xrightarrow{HX} R{-}\underset{X}{\underset{|}{C}}H{-}CH_2{-}(CH_2)_n{-}COOH + R{-}CH_2{-}\underset{X}{\underset{|}{C}}H{-}(CH_2)_n{-}COOH$$

A substituted acetylene is reacted with an α,ω-iodochloropolymethylene in the presence of sodium amide, and the resulting disubstituted acetylene is reacted first, with KCN to replace the Cl by CN, and then hydrolyzed to the acetylenecarboxylic acid I. This acid may be hydrogenated to the saturated or the ethylenic acids, II and III. When HX is added to the ethylenic acid III, both the potential halogenated acids are produced and must be separated by fractionation. Obviously, the structure of R and the number of methylene groups, *n*, will vary to conform to the structure of the desired acid.

b. Hydroxy acids. A few hydroxy acids, such as lactic acid,

$$CH_3—CHOH—COOH$$

from sour milk, are obtained from natural materials, but specific hydroxy acids are prepared by hydrolyzing the corresponding halogenated acids. They are prepared also by the *Reformatsky reaction.* This reaction is possible because the intermediate alkylzinc reacts faster with aldehydes and ketones than with esters.

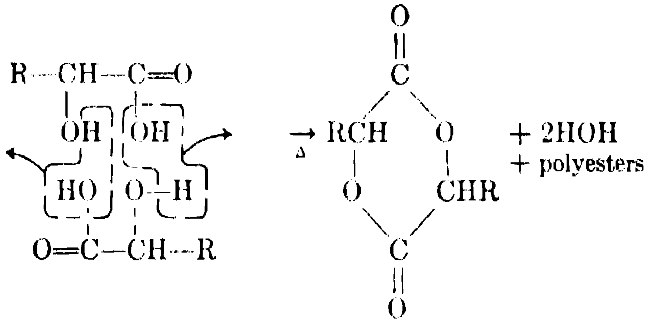


$$R_2C{=}O + BrCH_2—CO_2R \xrightarrow{Zn} \underset{\displaystyle OZnBr}{R_2C}—CH_2—COOR \xrightarrow{H_3O^+} \underset{\displaystyle OH}{R_2C}—CH_2—COOH$$

Thus, by using different aldehydes or ketones, and different α-halogenated esters, a variety of hydroxy acids may be prepared.

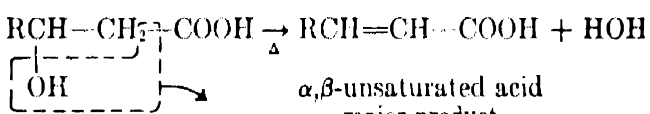
Some hydroxy acids are used in making resins and plastics (see Chapter 26). Upon pyrolysis, they lose water either *inter-* or *intra*molecularly. The δ-hydroxy acids yield six-membered ring lactones. The reactions of all but the β-hydroxy acids are really esterifications. The α-isomers yield a ring by the alcohol of one molecule esterifying the carboxyl group of another molecule, while the γ- and δ-isomers undergo *intramolecular* esterification.

α-Hydroxy acids



A lactide

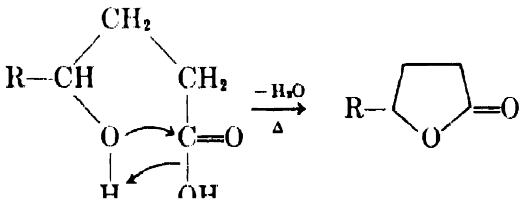
β-Hydroxy acids



$$\underset{\displaystyle OH}{RCH}—CH_2—COOH \xrightarrow{\Delta} RCH{=}CH—COOH + HOH$$

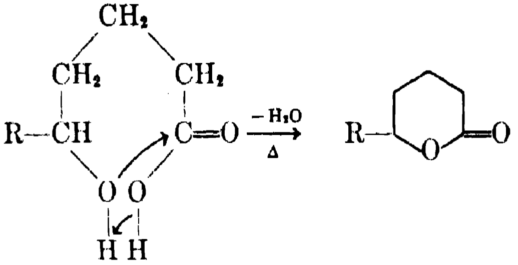
α,β-unsaturated acid
major product

γ-Hydroxy acids



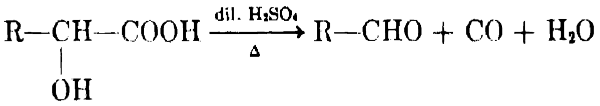
Five-membered
ring lactone
$\nu_{C=O} = 1760–1780\ cm^{-1}$

δ-Hydroxy acids



Six-membered
ring lactone
$\nu_{C=O}$ = 1735–1750 cm^{-1}

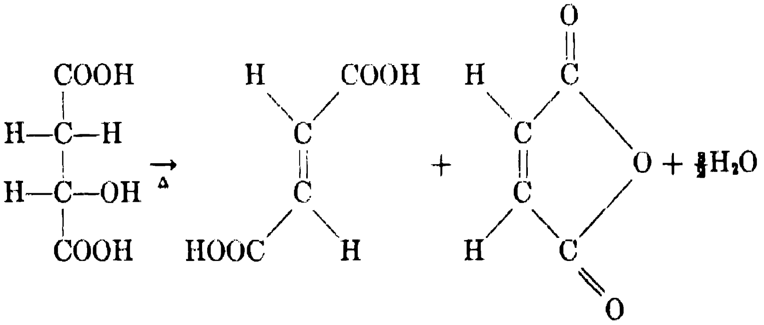
When α-hydroxy acids are boiled in dilute sulfuric acid, carbon monoxide and water are lost with the formation of an aldehyde.



$$\underset{\displaystyle OH}{\underset{|}{R\text{—}CH}}\text{—}COOH \xrightarrow[\Delta]{\text{dil. }H_2SO_4} R\text{—}CHO + CO + H_2O$$

The reaction can be used for the stepwise degradation of carbon chains. This is another example of the instability of compounds containing two groups, Y, attached to a single carbon atom, where Y may be OH, COOH, NH_2, etc. (cf. Sections 10.7, 10.8c, 15.5, and 15.6).

Some of the hydroxy polycarboxylic acids have important uses. Malic acid, obtained from apples, loses water upon pyrolysis to yield maleic anhydride and fumaric acid:

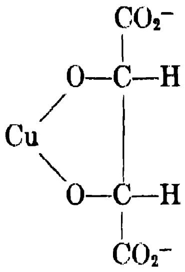


Malic acid Fumaric acid Maleic anhydride

Thus, malic acid reacts as a β-hydroxyacid, i.e., it loses water to yield an unsaturated acid. In this case, two geometric isomers, maleic and fumaric acids, are produced. The two COOH groups of maleic acid are close enough to form an intramolecular anhydride, but the *trans*-isomer, fumaric acid, does not. Maleic anhydride is used in making certain plastics (see Chapter 26) and for the Diels-Alder reaction (see Section 3.5).

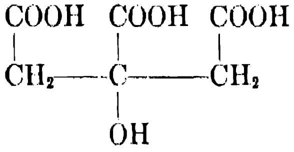
The monopotassium salt of tartaric acid, dihydroxysuccinic acid, HOOC—CHOH—CHOH—COOK, is sold as cream of tartar which is used

Fehling's solution (page 330). It forms an alkali-soluble copper complex, believed to have the structure,



since it migrates to the anode during electrolysis. In the past, tartaric acid was imported as a by-product of the European wine industry, but recently its commercial synthesis from maleic anhydride (made from benzene) has become economically successful.

Citric acid, a biologically important acid,



$$\begin{array}{ccc} COOH & COOH & COOH \\ | & | & | \\ CH_2 - & C & - CH_2 \\ & | & \\ & OH & \end{array}$$

is used extensively for forming soluble complexes of cations in ion exchangers. Through the use of ion exchangers, many salt mixtures have been separated on a large scale for the first time. For example, plutonium and uranium mixtures were separated for production of atomic bombs, and the rare earths are now available in pure form in pound quantities.

STUDY EXERCISES

1. Write three general equations for the preparation of carboxylic acids.

2. What are the common names of the first five fatty acids?

3. Compare the water solubilities of the first few members of the alkanes, alcohols, aldehydes, ketones, ethers, and carboxylic acids. Which ones are regarded as having practical solubilities in water?

4. Would one predict acetic acid to have a higher boiling point than acetyl chloride? Check this prediction with the facts.

5. Write equations for the reaction of propionic acid with (a) $SOCl_2$; (b) PCl_5; (c) KOH; (d) C_2H_5OH, H_2SO_4; (e) HN_3.

6. Write equations for the action of alcoholic potash upon α-chlorobutyric acid.

7. Name the following acids according to the Geneva system: (a) $(C_2H_5)_3C—COOH$; (b) $C_3H_7—CH(CH_3)—COOH$; (c) $(CH_3)_2CH—COOH$; (d) $CH_3CH_2CH_2CH(CH_3)—CH_2COOH$; (e) $[(CH_3)_2CH]_2CH—COOH$; (f) $(CH_3)_3C—CH_2—COOH$. Which ones are conveniently named as derivatives of acetic acid?

8. How would one prepare n-butyric acid from (a) ethyl butyrate, (b) n-propyl alcohol, (c) n-butyl alcohol, (d) n-butyraldehyde, (e) sodium butyrate, (f) propionic acid?

9. Write the structure of a dicarboxylic acid which upon pyrolysis would yield (a) *n*-butyric acid, (b) isobutyric acid, (c) isovaleric acid, (d) α-chloro-*n*-caproic acid.

10. How would one separate and isolate adipic acid from tetramethylene glycol?

11. Write the structure of 2,4-pentadienoic acid.

12. Write general equations for four methods of preparing aromatic carboxylic acids.

13. Write general equations for the formation of the ester, acid chloride, amide, and nitrile of *p*-toluic acid, starting with *p*-toluic acid, *p*-CH_3—C_6H_4—COOH.

14. Indicate the behavior of aqueous alkali upon benzamide, ethyl benzoate, and benzonitrile.

15. What sequence of laboratory reactions would you use to prepare (a) β-bromobutyric acid, (b) α-nitrobutyric acid, (c) α-hydroxybutyric acid, starting with butyric acid in each case.

16. Suggest ways of carrying out the following syntheses in the laboratory: (a) $HOCH_2$—CH_2—COOH from ethylene, (b) C_6H_5—CO—COOH from benzaldehyde, (c) *p*-nitrophenylacetic acid from *p*-nitrotoluene.

TEST QUESTIONS, Set 13

1. What weight of butyric acid could be made from 12.3 g of *n*-propyl bromide by forming a Grignard, carbonation of the Grignard, and hydrolysis of the addition product? Assume a 90 per cent yield in each of the three stages of the reaction.

2. Illustrate the series of reactions one could use to convert valeric acid to *n*-butanol, and to convert *n*-butanol to valeric acid.

3. How could a solid hydrocarbon be distinguished from a solid fatty acid?

4. What volume of 1.0 *N* alkali would be required to neutralize 2.5 g of acetic acid?

5. A sample of a monocarboxylic acid weighing 0.2100 g required 18.10 ml of *N*/10 KOH solution for neutralization. What is the molecular weight of the acid?

6. How could the presence of formic acid in acetic acid be detected?

7. What series of reactions would be used to prepare α-bromopropionic acid from ethyl alcohol? Is there a route which does not involve halogenation of propionic acid?

8. Should a saturated alcohol be any more soluble in aqueous potassium carbonate than in water? Why or why not? Should an acid, valeric acid, for example, be any more soluble in aqueous potassium carbonate than in water? Why, or why not?

9. Indicate the sequences of laboratory reactions one could use to prepare (a) trichloroacetic acid from methanol, (b) butyric acid from ethanol, (c) succinic acid from ethyllene, (d) succinic acid from *n*-propy alcohol.

10. When oxalic acid is heated directly, it does not char. How could one prove the presence of carbon in the compound?

11. What weight of potassium permanganate would be required to oxidize 10 g of oxalic acid to CO_2 in sulfuric acid? In which role does oxalic acid have the larger equivalent weight, as a reducing agent or as an acid?

12. How could one distinguish by qualitative tests (a) oxalic acid from acetic acid, (b) malonic acid from succinic acid?

13. Explain the greater acid strength of nitric acid over nitrous acid in terms of resonance theory.

14. Twenty-five milliliters of 0.2 *N* NaOH are required to neutralize 0.44 g of a monocarboxylic acid. The acid will give only a mono α-bromination product. What is its structure?

15. How could one explain the fact that trichloroacetic acid is a much stronger acid than acetic acid, and trimethylacetic acid is weaker than acetic acid? On this basis, predict the stronger acid in the following pairs:

(a) $Br—CH_2—COOH$ and $Cl—CH_2—COOH$
(b) $CH_3—CHCl—COOH$ and $Cl—CH_2—CH_2—COOH$

16. A neutral compound X, $C_4H_8O_2$, reduces Tollens' reagent, liberates H_2 when treated with sodium metal, and slowly gives a positive iodoform test. What is a possible structural formula for X?

17. What weight of potassium dichromate would be required to oxidize 1 mole of *p*-chlorotoluene to *p*-chlorobenzoic acid in acid solution?

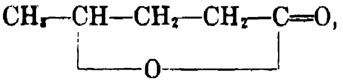
18. Saccharin is made by heating *o*-carboxybenzenesulfonamide. What series of reactions can be used to prepare saccharin, starting with toluene?

19. Give equations for the preparation of acetylsalicylic acid (aspirin), and of methyl salicylate, starting with phenol in each case.

20. Which should be the better solvent for benzoic acid, ethyl ether or petroleum ether? Explain the basis of your prediction.

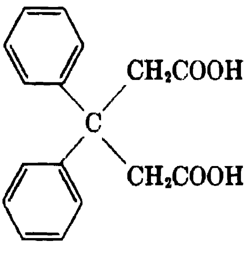
21. Acetophenone yields chloroform when treated with chlorine in aqueous alkali, but 2,6-dimethylacetophenone only produces 2,6-dimethyl-α,α,α-trichloroacetophenone under the same conditions. Offer a possible explanation for the difference in behavior of the two compounds.

22. How could one distinguish by qualitative test-tube experiments (a) acrylic acid, $CH_2=CH—COOH$, from propionic acid; (b) acrylic acid from acetylenecarboxylic acid?

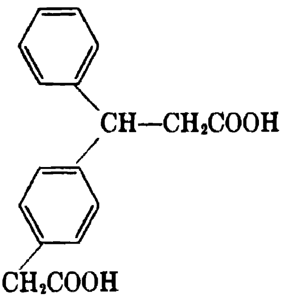
23. What sequence of laboratory reactions could one use to prepare: (a) β-bromopropionic acid from acetic acid; (b) γ-bromovaleric acid from valeric acid? Then how would one prepare γ-valerolactone,  $CH_3—CH—CH_2—CH_2—C=O$ (with O bridging CH and C=O), using the γ-bromovaleric acid?

24. Propose a mechanism for the loss of CO plus H_2O from an α-hydroxy acid when heated in sulfuric acid.

25. Two isomeric compounds I and II were prepared and characterized. What n.m.r. spectral characteristics would you seek in order to differentiate the two? Should there by any significant difference between the ratios of K_1 and K_2 for I and II, where K_1 and K_2 refer to the first and second acid dissociation constants?



I



II

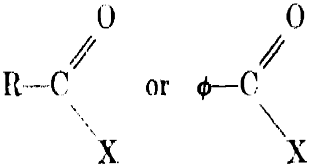
26. A compound A, $\nu_{C=O}$ 1742 cm^{-1}, is insoluble in water, dilute acid, and base. It does not give a 2,4-dinitrophenylhydrazone or affect the color of aq. ceric nitrate. After three hours refluxing in dilute base, nothing can be extracted with ether from the alkaline solution. A product B can be isolated from the reaction mixture after acidification. Product B, equivalent weight 130 ± 2, turns aq. ceric nitrate red and gives a positive iodoform test. Deduce the structure of A from these observations.

27. A compound R, $C_{10}H_{12}O_2$, has infrared absorption bands at 1685 and 1250 cm^{-1}. It is insoluble in dilute acid and base. It does not reduce Tollens' reagent but forms a 2,4-dinitrophenylhydrazone. Upon vigorous oxidation it yields an acidic product, $C_9H_8O_5$, which forms an acid anhydride upon heating. Treatment of R with sodium hypobromite gives a different acid which, when heated with soda-lime, yields *p*-$CH_3O—C_6H_4—CH_3$. Propose a structural formula for R.

14

Acid Halides and Anhydrides

Acid halides are compounds in which the OH group of a carboxylic acid has been replaced by a halogen atom. This gives them the general structure



where X is a halogen atom. The RCO or ϕCO group is sometimes called an *acyl group*.

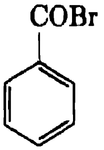
14.1 NOMENCLATURE OF ACID HALIDES

The I.U.C. system of naming acid halides uses the suffix *-oyl* in place of the *-e* of the *-ane* ending of alkanes, followed by the name of the halogen. Again, the carbon atoms are numbered from the acyl carbon atom. The common names of acid halides are derived from those of the corresponding acids, with the name of the halogen added. The carbon atoms in the chain are lettered according to the Greek alphabet. A few illustrations of both systems of naming acid halides are given in Table 14.1.

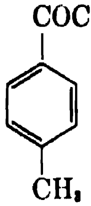
TABLE 14.1. ACID HALIDE NOMENCLATURE

Structure	I.U.C. Name	Common Name
(H—COCl) unstable	Methanoyl chloride	Formyl chloride
CH_3—COBr	Ethanoyl bromide	Acetyl bromide
CH_3—CHCl—CH_2—COF	3-Chlorobutanoyl fluoride	β-Chlorobutyryl fluoride

The aromatic acid halides are named after the corresponding acids:



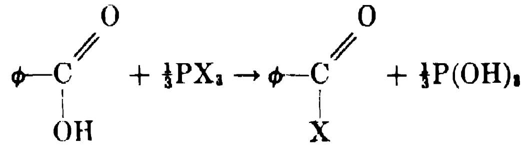
Benzoyl bromide



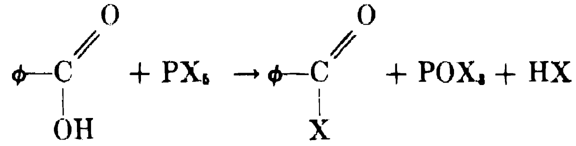
p-Toluyl chloride

14.2 PREPARATION OF ACID HALIDES

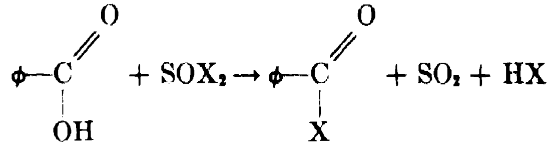
The acid halides, aromatic as well as aliphatic, are prepared from the corresponding acids by treatment with the usual reagents used to replace OH by X.



$$\phi\text{—}\overset{\displaystyle O}{\underset{\displaystyle OH}{C}} + \tfrac{1}{3}PX_3 \rightarrow \phi\text{—}\overset{\displaystyle O}{\underset{\displaystyle X}{C}} + \tfrac{1}{3}P(OH)_3$$



$$\phi\text{—}\overset{\displaystyle O}{\underset{\displaystyle OH}{C}} + PX_5 \rightarrow \phi\text{—}\overset{\displaystyle O}{\underset{\displaystyle X}{C}} + POX_3 + HX$$



$$\phi\text{—}\overset{\displaystyle O}{\underset{\displaystyle OH}{C}} + SOX_2 \rightarrow \phi\text{—}\overset{\displaystyle O}{\underset{\displaystyle X}{C}} + SO_2 + HX$$

In general, the sodium salts may be used in place of the organic acids.[1]

14.3 PHYSICAL AND CHEMICAL PROPERTIES OF ACID HALIDES

The acid halides are nonassociated substances, and therefore, they are lower boiling than the corresponding acids. For example:

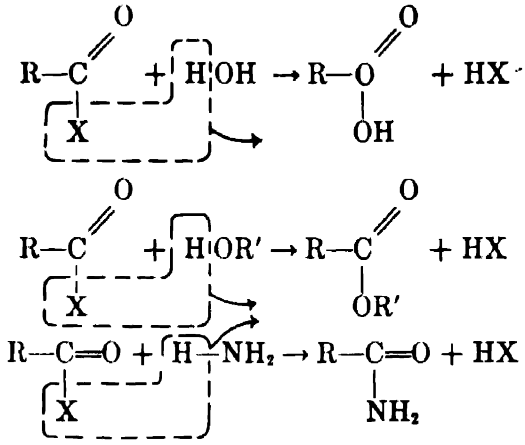
	Boiling Point of Acid	*Boiling Point of Acid Chloride*
Acetic acid	118°	51°
Benzoic acid	249°	197°

The acid halides do not dissolve in water, but they hydrolyze rapidly to yield the acid and halide ion. Owing to this ease of hydrolysis, the acid halides have few important industrial or domestic uses other than as intermediates in organic synthesis. Therefore, only the simplest ones are commercially available. In this respect, their major use is to serve as acylating agents, i.e., the replacement of active H's by acyl groups, for which most often the CH_3CO or C_6H_5CO groups will serve, or as intermediates in multistep syntheses. With this in mind, we will consider some of their more common chemical properties.

---

[1] A good method of preparing acid halides and anhydrides is to use oxalyl chloride, Cl—CO—CO—Cl, with carboxylic acid sodium salts. (R. Adams and L. H. Ulich, *J. Am. Chem. Soc.*, **42**, 599 (1920); A. W. Schrecker and P. B. Maury, *ibid.*, **76**, 5803 (1954).) However, because of the ready availability of the reagents used above, rarely does a chemist resort to the use of oxalyl chloride.

a. Acylation. See Section 15.4 concerning mechanism.


R—C(=O)X + H—OH → R—O(=O)—OH + HX
R—C(=O)X + H—OR′ → R—C(=O)—OR′ + HX
R—C=O(X) + H—NH₂ → R—C=O(NH₂) + HX

Observe that HX is produced in each case, and by measuring the quantity of acid liberated, one can use the reactions for the quantitative determination of the number of active H's in a molecule. This application will be used later. When alkali or some other base is used to take up the HX, the reaction is called the *Schotten-Baumann reaction.*

b. Reduction.

$$R\text{—}COCl + H_2 \xrightarrow{Pd} R\text{—}CHO + HCl$$

$$R\text{—}COCl + LiAlH_4 \rightarrow R\text{—}CH_2OH$$

These reactions are illustrated for the chlorides because the chlorides are by far the most common. The reduction to aldehydes, known as the *Rosenmund reduction*, was discussed in Section 12.2c.

c. Degradation.

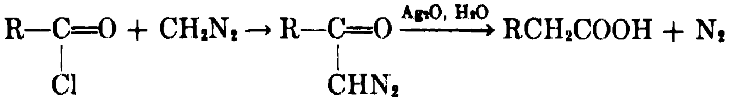
$$R\text{—}COCl + HN_3 + H_2O \rightarrow R\text{—}NH_2 + HCl + CO_2 + N_2$$

This reaction is carried out just as it is with carboxylic acids, discussed on page 347.

$$R\text{—}COCl \xrightarrow[\Delta]{Ag_2O,\ X_2} R\text{—}X + CO_2 + AgCl$$

This reaction may be preferred to the Hunsdiecker reaction when the acid chloride can be prepared more conveniently than the silver salt.

d. Arndt-Eistert reaction. See page 349.



$$\underset{\displaystyle Cl}{R—C{=}O} + CH_2N_2 \rightarrow \underset{\displaystyle CHN_2}{R—C{=}O} \xrightarrow{Ag_2O,\ H_2O} RCH_2COOH + N_2$$

This reaction may be used as a method of lengthening the carbon chain by one carbon atom. The diazoketone is also useful as an intermediate in the synthesis of other types of compounds:

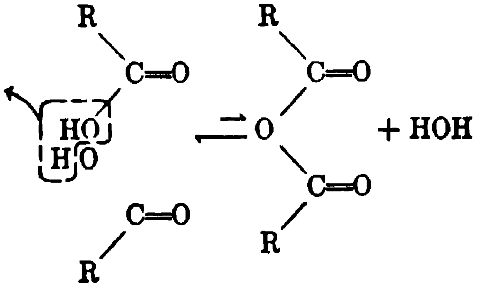
$R—CO—CHN_2 + HCl \rightarrow R—CO—CH_2Cl$ Synthesis from the methyl ketone by monochlorination impractical.

$R—CO—CHN_2 + HOR' \rightarrow R—CH_2—COOR'$

$R—CO—CHN_2 + HNH_2 \rightarrow R—CH_2—CONH_2$

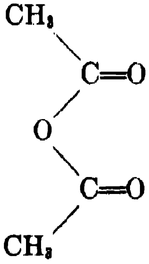
14.4 ACID ANHYDRIDES

Acid anhydrides are just what this name implies, the condensation products of acids through the loss of water.

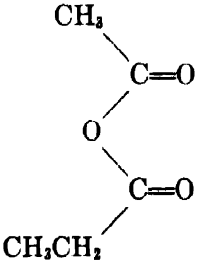


An acid anhydride

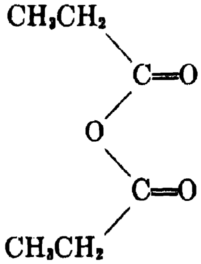
The R's may or may not be alike, and may even be joined. The names of acid anhydrides stem from the names of the two acyl groups attached to the center oxygen atom.



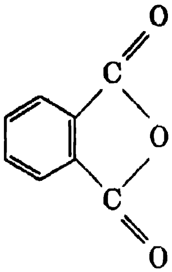
Acetic anhydride



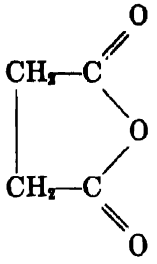
Acetic propionic anhydride



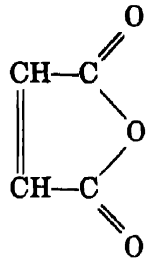
Propionic anhydride



Phthalic anhydride



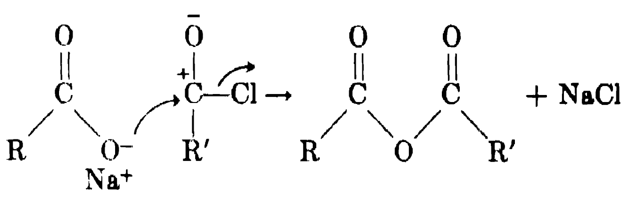
Succinic anhydride



Maleic anhydride

Notice that when the acyl groups are alike, the name is given only once, as in acetic anhydride.

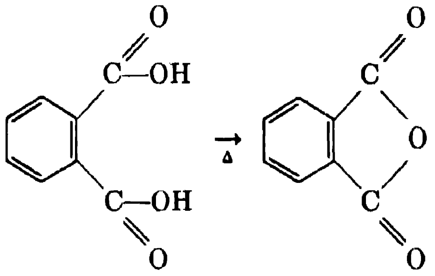
Acid anhydrides are prepared by reacting acid halides with sodium salts of carboxylic acids.



This reaction was given earlier on page 344. Like the acid halides, the acid anhydrides have little industrial use and only the simplest ones are produced on a commercial scale. Other than for research studies, the acyl groups will usually be alike. Furthermore, mixed anhydrides tend to disproportionate into two corresponding simple anhydrides.

$$2R—CO—O—CO—R' \xrightarrow[\Delta]{} (RCO)_2O + (R'CO)_2O$$

This makes it difficult to purify the unsymmetrical anhydrides. The intramolecular anhydrides are usually prepared by simple pyrolysis of the dibasic acids.



Acid anhydrides are nonassociated substances and boil at higher temperatures than the respective acids because their molecular weights are almost twice those of the acids, and this is too big a factor for hydrogen bonding to overcome. For example, acetic acid boils at 118°, and acetic anhydride boils at 138°.

Acid anhydrides are used for acylations in preference to acid halides, because the reactions are not as vigorous and are more easily controlled. They react to replace hydrogen atoms, attached to nitrogen or oxygen, by acyl groups (see Section 15.4 for mechanism).

$$(RCO)_2O + H{-}OH \rightarrow R{-}COOH + R{-}COOH$$

$$(RCO)_2O + H{-}OR' \rightarrow R{-}COOH + R{-}COOR'$$

$$(RCO)_2O + H{-}NR_2 \rightarrow R{-}COOH + R{-}CONR_2$$

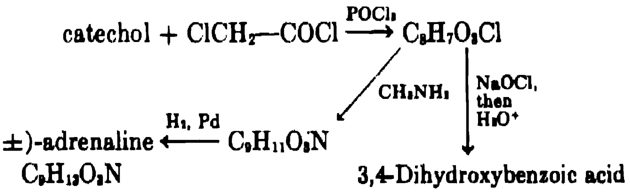
In these reactions, an organic acid is always one of the products, and as with the acid halides, measurement of the quantity of acid liberated may be used as a method of determining the number of hydroxyl or amino groups in a compound (see Section A-4b).

STUDY EXERCISES

1. Give equations for the general methods of preparing acid halides and anhydrides.
2. What would one expect to be the order of relative boiling points of propionic acid, propionyl chloride, and propionic anhydride? Check your prediction with the facts.
3. Indicate by equations the reaction of (a) propionyl chloride with isopropyl alcohol, (b) *n*-butyric anhydride with ammonia.
4. What is the difference between the terms *acylation* and *acetylation?*

TEST QUESTIONS, Set 14

1. How could one distinguish, by qualitative test-tube experiments, acetyl bromide from bromoacetic acid?
2. What is the molecular weight of a trihydric alcohol if 0.46 g of it is acetylated with acetic anhydride, and 15 ml of 1 *N* NaOH are required to neutralize the liberated acetic acid? See Section A-4b for help, if needed.
3. How could one prepare α-bromobutyryl bromide from butyric acid?
4. Why is acetyl chloride more reactive than ethyl chloride toward nucleophilic reagents? (See Section 15.4 for aid, if necessary.)
5. How could one determine the acetic acid content of a solution of acetic acid in acetic anhydride?
6. Indicate by an equation the reaction of valeryl bromide with alc. KOH.
7. What series of laboratory reactions, starting with ethyl bromide, would you use to prepare maleic anhydride?
8. The structure of the *adrenal* hormone *adrenaline* was proved by its synthesis through the following reactions:



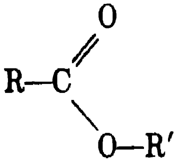
$$\begin{tikzcd}
\text{catechol} + ClCH_2{-}COCl \arrow[rr, "POCl_3"] & & C_8H_7O_3Cl \arrow[dl, "CH_3NH_2"] \arrow[d, "\text{NaOCl, then } H_3O^+"] \\
(\pm)\text{-adrenaline} & C_9H_{11}O_3N \arrow[l, "{H_2, Pd}"'] & \text{3,4-Dihydroxybenzoic acid} \\
C_9H_{13}O_3N & &
\end{tikzcd}$$

What is the structural formula of adrenaline?

15

Esters

Esters are alkyl or aryl derivatives of both inorganic and organic acids. Hence, esters of carboxylic acids have a general structure such as

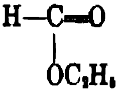
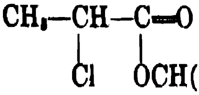
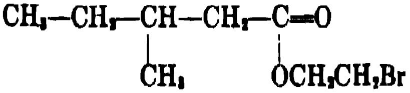


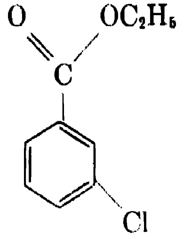
where the R's may be aliphatic or aromatic. Up to Section 15.8 all references made to esters will be esters of carboxylic acids. Esters of inorganic acids will be discussed in Section 15.8.

15.1 NOMENCLATURE

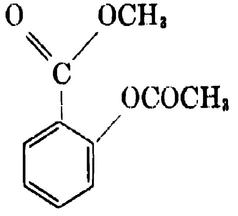
An ester is named on the basis of the corresponding acid by changing *-ic* to *-ate* and preceding this with the name of the alkyl group attached to the hydroxyl oxygen atom. For illustration, a few examples are given in Table 15.1.

TABLE 15.1. ESTER NOMENCLATURE

Structure	I.U.C. Name	Common Name
 $\mathrm{H-\underset{OC_2H_5}{C}=O}$	Ethyl methanoate	Ethyl formate
 $\mathrm{CH_3-\underset{Cl}{CH}-\underset{OCH(CH_3)_2}{C}=O}$	Isopropyl 2-chloropropanoate	Isopropyl α-chloropropionate
 $\mathrm{CH_3-CH_2-\underset{CH_3}{CH}-CH_2-\underset{OCH_2CH_2Br}{C}=O}$	2-Bromoethyl 3-methylpentanoate	β-Bromoethyl β-methylvalerate

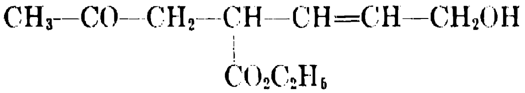


Ethyl *m*-chlorobenzoate



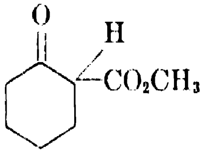
Methyl *o*-acetoxybenzoate
or
methyl acetylsalicylate

It is frequently awkward to name a compound as a derivative of the acid, and it is simpler to regard the COOR group as a substituent. In this case, the COOR group is called a carboalkoxy group. For illustration,



$$CH_3\text{—}CO\text{—}CH_2\text{—}\underset{\displaystyle CO_2C_2H_5}{\underset{|}{C}H}\text{—}CH{=}CH\text{—}CH_2OH$$

4-Carboethoxy-6-keto-2-heptenol
or
1-hydroxy-4-carboethoxy-2-heptenone-6
or even,
4-carboethoxy-2-heptene-1-ol-6-one



2-Carbomethoxy-cyclohexanone

15.2 PREPARATION

Esters are prepared by the acylation of alcohols as first shown in Section 10.6c. Either organic acids, acid halides, or anhydrides may be used.

$$R'COOH + R^2OH \xrightleftharpoons{\text{acid}} R'COOR^2 + HOH \qquad (1)$$

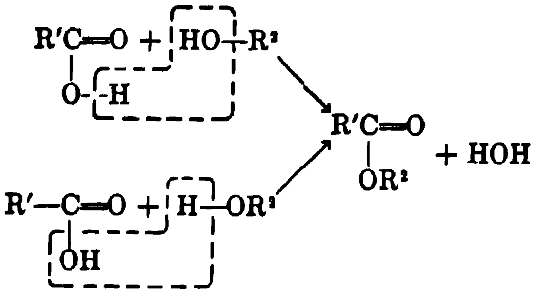
$$R'COX + R^2OH \longrightarrow R'COOR^2 + HX$$

$$(R'CO)_2O + R^2OH \longrightarrow R'COOR^2 + R'COOH$$

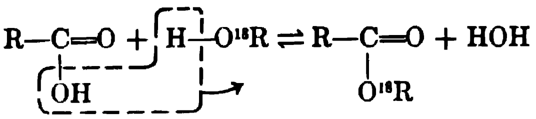
Reaction (1) is commonly referred to as *esterification*. It is reversible and catalyzed in both directions by acid. When it is desired to prepare an ester, the equilibrium is shifted to the right by the addition of sulfuric acid. Sulfuric acid not only serves as a catalyst, but combines with the water formed to produce a sulfuric acid hydrate. When the purpose is to hydrolyze the ester, alkali is added because it forms a salt of the organic acid and prevents the latter from reacting, i.e., it shifts the equilibrium completely to the left.

As a means of determining the mechanism of esterification, it is desirable to know whether the alkoxyl oxygen of the ester is that of the alcohol or of the acid. That is, in the elimination of water, does the OH come from the alcohol and the H from the acid, or does the OH come from the acid and the H from the alcohol?

or

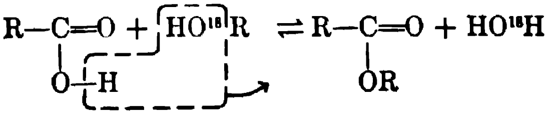


This question was answered conclusively by using alcohols containing isotopic oxygen in place of normal oxygen-16.



(2)

$$R-\underset{OH}{\underset{|}{C}}=O + H-O^{18}R \rightleftharpoons R-\underset{O^{18}R}{\underset{|}{C}}=O + HOH \qquad (2)$$



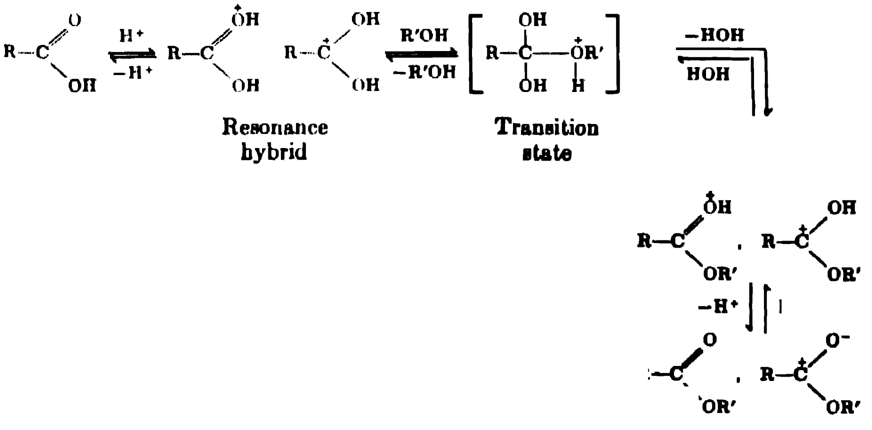
(3)

$$R-\underset{OH}{\underset{|}{C}}=O + HO^{18}R \rightleftharpoons R-\underset{OR}{\underset{|}{C}}=O + HO^{18}H \qquad (3)$$

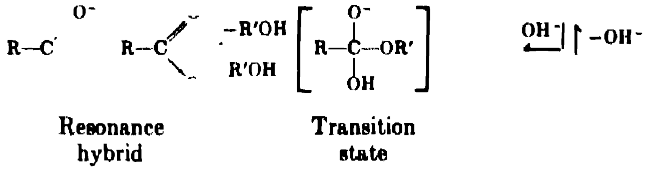
Hence, if the OH comes from the alcohol as in (3), the heavy oxygen would end up in the water, but if the OH comes from the acid as in (2), the oxygen-18 would end up in the ester. By experiment, it was found that primary alcohols react by mechanism (2), secondary alcohols by (2) and (3), and tertiary alcohols predominantly by mechanism (3). The same situation occurs for the hydrolysis of esters. Some hydrolyze by scheme (2), some by (2) and (3), and some solely by (3). This variation in mechanism is due to steric requirements. With a given acid, RCH_2COOH, the relative rates of esterification by alcohols decrease in the order, primary > secondary > tertiary. For a given carbinol, RCH_2OH, the relative rates of reaction with acids is in the order $RCH_2COOH > R_2CHCOOH > R_3C—COOH$.

Esterification is a reversible reaction, and in the absence of steric effects the reaction mechanism is close to the following:

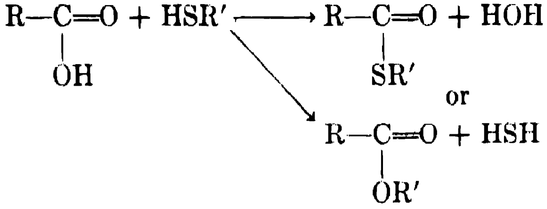
Acid catalyzed esterification or hydrolysis:



Base catalyzed hydrolysis:



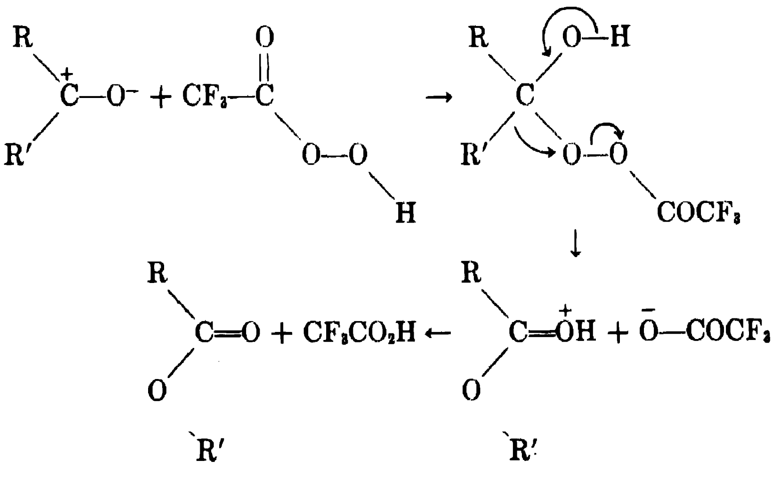
Even before the experiments with isotopic oxygen were done, it was deduced from two indirect lines of reasoning that, in esterification, the OH of water comes from the acid. First, it is known that when the OH of alcohols is to be replaced, tertiary alcohols react the fastest, and when the hydroxyl hydrogen atom is to be replaced, primary alcohols react the fastest. Since simple organic acids are esterified most rapidly with primary alcohols, it was assumed that the hydrogen comes from the alcohol in esterification. Secondly, if a thioalcohol, RSH, is used in place of an alcohol, it is easy to follow the course of the reaction.



$$\underset{\textstyle OH}{R\text{—}C\text{=}O} + HSR' \longrightarrow \underset{\textstyle SR'}{R\text{—}C\text{=}O} + HOH \quad \text{or} \quad \underset{\textstyle OR'}{R\text{—}C\text{=}O} + HSH$$

Obviously, it was easy to determine whether H_2O or H_2S was liberated, and here it was found that H_2O was formed. If one assumes the mechanism for alcohols and thioalcohols to be the same, the same conclusion is reached regarding the mechanism of esterification as was later found using isotopic oxygen.

A less widely used method of preparing esters is through the oxidation of ketones with a peracid, called the *Baeyer-Villiger* reaction.



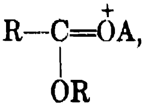
The migrating group of the ketone is the one best able to carry a positive charge.

The reaction finds application as a step in a multistep synthesis for converting a ketone to an ester or acid group or for the cleavage of a ketone. Methyl ketones, it will be recalled, are cleaved by the haloform reaction.

15.3 PHYSICAL PROPERTIES

Esters cannot form hydrogen bonds, and therefore esters have lower boiling points than the respective acids, as long as the alkoxyl group is not too large. Thus, methyl and ethyl esters boil at lower temperatures than the corresponding acids.

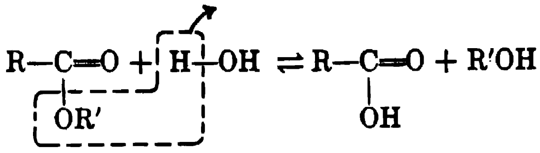
	Boiling Point of Acid	*Boiling Point of Ethyl Ester*
C_2H_5COOH	141°	99°
C_6H_5COOH	249°	213°
$C_6H_{11}COOH$	233°	196°

Although water may form hydrogen bonds with esters, the esters lack OH groups for forming hydrogen bonds with water, and this absence of coassociation prevents esters from having large solubilities in water. For example, the first four carboxylic acids, formic to butyric, are soluble in water in all proportions, but their ethyl esters are only sparingly soluble (see the data in Section 13.3). However, since esters may form oxonium ions with strong acids,  $R{-}\underset{\displaystyle OR}{\underset{|}{C}}{=}\overset{+}{O}A$, where A is a strong acid, esters are appreciably soluble in concentrated sulfuric acid, as are most oxygen-containing compounds.

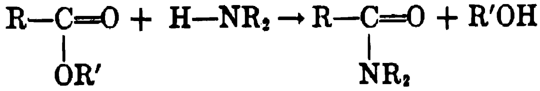
Esters are characterized by having very pleasant odors, resembling those of fruits or flowers, and frequently they are the aromatic components of natural and synthetic perfumes. The greatest use of esters is as solvents in the lacquer industry. Some naturally occurring esters of animal or vegetable origin from high-molecular-weight fatty acids and monohydric alcohols are valuable waxes (compare with the petroleum waxes, page 79). *Beeswax*, from the honeycomb of bees, is chiefly myricyl palmitate, $C_{15}H_{31}CO_2C_{30}H_{61}$. *Spermaceti*, a crystalline wax from sperm oil, is chiefly cetyl palmitate, $C_{15}H_{31}CO_2C_{16}H_{33}$. *Carnauba* wax, a coating on the leaves of a species of palm, contains myricyl cerotate, $C_{26}H_{53}CO_2C_{30}H_{61}$.

15.4 CHEMICAL PROPERTIES

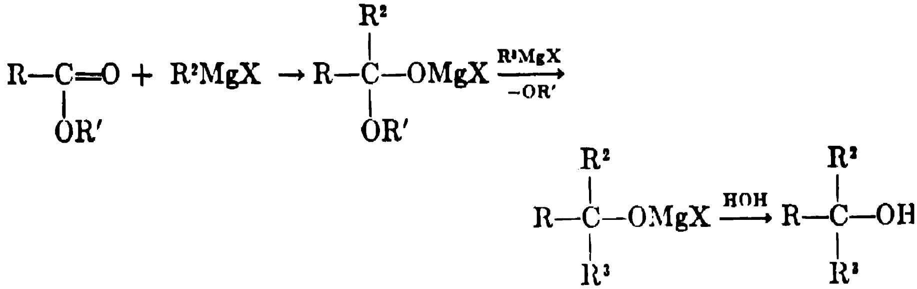
a. Displacement reactions. Esters undergo several useful displacement reactions.



$$R-\underset{OR'}{C}=O + H-OH \rightleftharpoons R-\underset{OH}{C}=O + R'OH$$

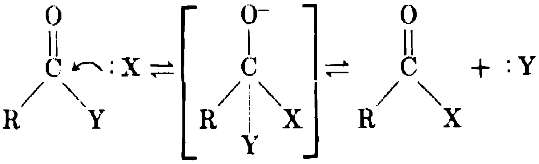


$$R-\underset{OR'}{C}=O + H-NR_2 \rightarrow R-\underset{NR_2}{C}=O + R'OH$$

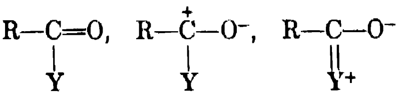


$$R-\underset{OR'}{C}=O + R^2MgX \rightarrow R-\overset{R^2}{\underset{OR'}{C}}-OMgX \xrightarrow[-OR']{R^3MgX} R-\overset{R^2}{\underset{R^3}{C}}-OMgX \xrightarrow{HOH} R-\overset{R^2}{\underset{R^3}{C}}-OH$$

All the acyl classes of compounds undergo displacement reactions similarly as do the alkyl halides (page 230).



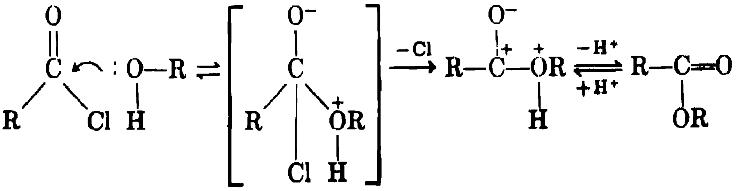
The acyl compound is a resonance hybrid of three major forms I, II, and III.



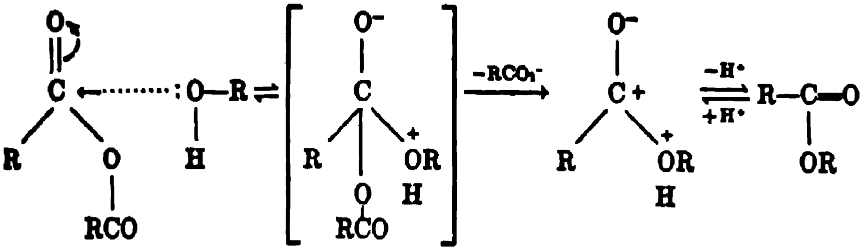
$$R-\underset{Y}{C}=O, \quad R-\overset{+}{\underset{Y}{C}}-O^-, \quad R-\underset{\substack{\| \\ Y^+}}{C}-O^-$$

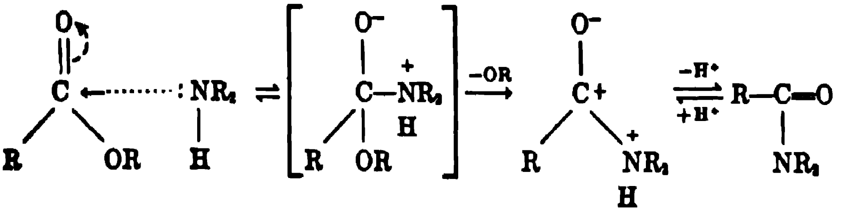
I II III

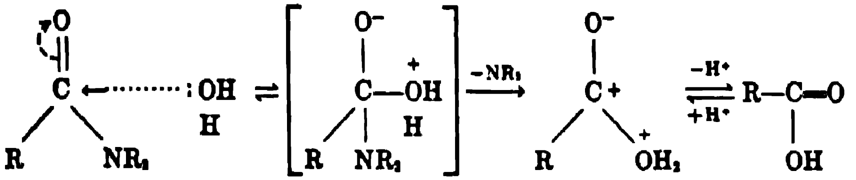
The contribution of III decreases with increasing electronegativity and decreasing electron-donor character of Y. Thus, the net contribution of III increases approximately in the order Y = F, Cl, Br, I, OCOR, OR, OH, NH_2. The smaller the contribution of III, the more readily will the acyl compound react with nucleophilic substances.



(4)


(5)


(6)

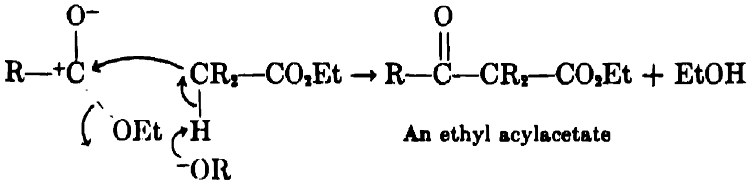

(7)

Reactions (4) and (5) are so vigorous as to be practically irreversible; reactions (6) and (7) are reversible, with the normal position of equilibrium lying on the right. Thus, it is convenient to carry out ammonolysis of esters (6) or hydrolysis of amides (7) in the laboratory, but not the alcoholysis of amides (6 in reverse) or the ammonolysis of acids (7 in reverse). The latter processes require forceful conditions of elevated temperatures and pressures which are easily accommodated in industrial laboratories.

b. Reduction of esters. Esters are conveniently reduced to alcohols with lithium aluminum hydride, sodium metal, or catalytic hydrogenation.

$$R{-}COOR' \xrightarrow{\text{R.A.}} R{-}CH_2OH + R'OH \qquad \text{R.A.} \quad \begin{array}{l} LiAlH_4 \\ \text{Na in alcohol} \\ H_2,\ Ni \end{array}$$

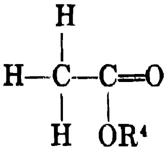
c. Claisen condensation. One of the most useful reactions of esters is the Claisen condensation. In the presence of a strong base, such as sodium alkoxide, sodium amide, or sodium hydride, the *alpha* hydrogen of one ester molecule splits out ROH with the alkoxyl group of another ester molecule. For example, with ethyl esters, an ethyl acylacetate would be formed as follows:


An ethyl acylacetate

The acylacetates are important intermediates in the preparation of substituted ketones and carboxylic acids as discussed in Section 15.5.

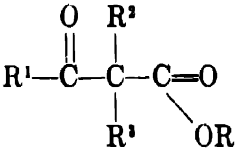
15.5 ACETOACETIC ESTERS

In the equation for a Claisen condensation given above, a general structure of an acylacetate ester was given. It is really a substituted acetate,



$$\mathrm{H{-}\overset{H}{\underset{H}{C}}{-}\underset{OR^4}{C}{=}O}$$

An unsubstituted acetate

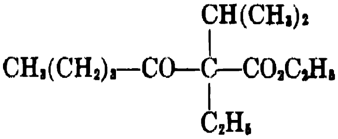
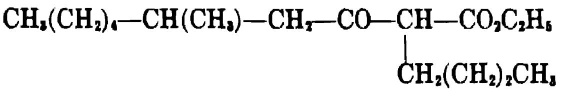


$$\mathrm{R^1{-}\overset{O}{\overset{\|}{C}}{-}\overset{R^2}{\underset{R^3}{C}}{-}C(=O){-}OR^4}$$

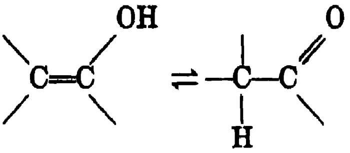
An acyldialkylacetate

in which R's and an acyl group have been substituted for the *alpha* H's of a simple acetate ester. The structure of R^4 is immaterial and is usually an ethyl group, and R^1, R^2, and R^3 may be simple or complex groups or even hydrogen atoms. The acylacetates are named in the regular fashion of naming esters, i.e., name the alkoxyl alkyl group then give the name of the acid, modified to end in *-ate*. The acyl group is named on the basis of the corresponding acid too. A few illustrations are given in Table 15.2.

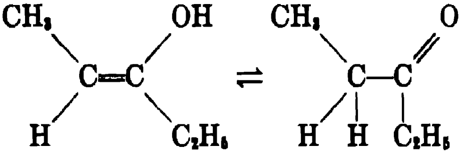
TABLE 15.2. NOMENCLATURE OF ACETOACETIC ESTERS

Structure	Name
$CH_3{-}CH_2{-}CO{-}C(CH_3)_2{-}COOC_2H_5$	Ethyl α,α-dimethylpropanoylacetate
 $$CH_3(CH_2)_3{-}CO{-}\overset{CH(CH_3)_2}{\underset{C_2H_5}{C}}{-}CO_2C_2H_5$$	Ethyl α-isopropyl-α-ethylpentanoylacetate
 $$CH_3(CH_2)_4{-}CH(CH_3){-}CH_2{-}CO{-}\underset{CH_2(CH_2)_2CH_3}{CH}{-}CO_2C_2H_5$$	Ethyl α-*n*-butyl-β-methyloctanoylacetate

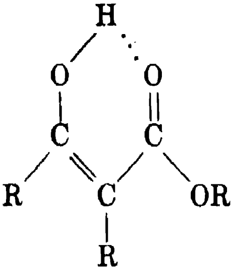
Very often the acyl group is the acetyl group; hence, these acylacetates as a class are called *acetoacetate esters*. Not only are they useful for synthesizing substituted acids and ketones but they are interesting because of their tautomeric nature. In Section 4.5 tautomerism was introduced and discussed, and it was pointed out that the keto-enol equilibrium is a common tautomeric system.



With just hydrogen atoms or simple alkyl groups attached to the carbon atoms, i.e.,

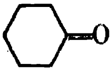


the bond energies make the keto form so much more stable that barely measurable amounts of the enol form exist at normal temperatures. When certain groups are a part of these structures, however, the relative stabilities are altered, and the equilibrium may shift, even completely toward the enol side (see Table 15.3). In the case of the acetoacetic esters, as with 1,3-diketones, it is possible for intramolecular hydrogen bonding to occur in the enolic forms.

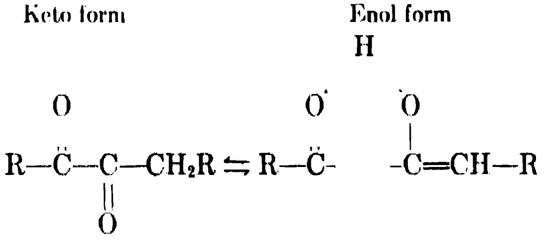


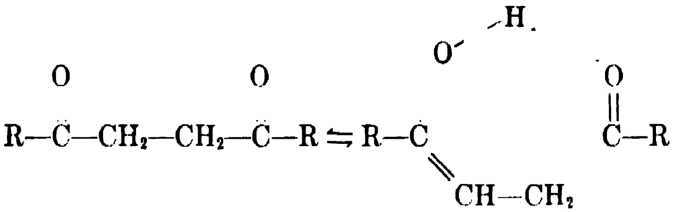
This stabilizes the enol tautomer with respect to the keto tautomer, and as a result, these compounds have appreciable enol contents. For illustration, the enol contents of several substances are given in Table 15.3.

TABLE 15.3. ENOL CONTENT OF SOME KETONES

Structure	Name	Enol Content (%)
$CH_3—CO—CH_3$	Acetone	0.000015 (liq.)
	Cyclohexanone	1.18
$C_2H_5O—CO—CH_2—CO_2C_2H_5$	Diethyl malonate	< 1.0
$CH_3—CO—CH_2—CO_2C_2H_5$	Ethyl acetoacetate	7.7 (liq.)
$CH_3—CO—CH_2—CO—CH_3$	Acetylacetone	76 (liq.)
$\phi—CO—CH_2—CO—CH_3$	Benzoylacetone	89 (liq.)
$\phi—CO—CH_2—CO—\phi$	Dibenzoylmethane	100

This is an excellent demonstration of the stabilizing effect of hydrogen bonding. If the keto groups are adjacent or separated by more than one carbon atom, the enol contents are negligible because the ring structures of five or more than six atoms are not very stable.



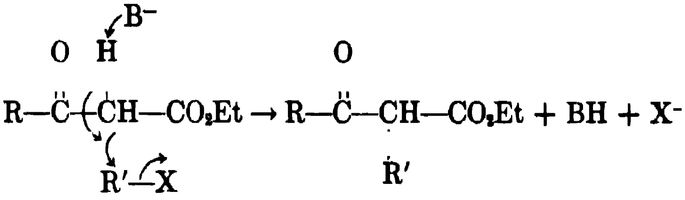


Hence these compounds have no more enolic character than simple ketones and esters. Since the 1,2- and 1,4-diketones are not enolic, this shows that the enolic content of 1,3-diketones is due chiefly to intramolecular hydrogen bonding and not to a twofold chance of tautomerization (owing to the presence of two C═O groups).

The simultaneous presence of enol and keto forms in a sample of an acetoacetic ester is known from the fact that it exhibits both ketonic and enolic properties. For example, a sample of an acetoacetic ester will form a bisulfite addition compound, an oxime, and a cyanohydrin, and will exhibit other typical ketonic properties. This is not due to the ester C═O group, because simple esters do not undergo these ketonic reactions. At the same time, another sample of the same material will add halogens, showing the presence of a C═C group, will give a deep coloration with aqueous ferric chloride, and will dissolve in alkali, the latter properties being typical of enols. Enols are weak acids with K_a's in the range 10^{-9} to 10^{-13}.

The separate enol and keto forms of acetoacetic ester were isolated by Knorr in 1911. By evaporating an ether solution of the ester at −80° under reduced pressure, the keto form was obtained in crystalline form. In this solvent, essentially only the keto form exists. The sodium salt of ethyl acetoacetate was carefully decomposed by dry hydrogen chloride to yield the liquid enol. The tautomers are stable for a long period when kept in quartz vessels at −78° but at room temperature they rapidly change to the equilibrium mixture.

In the Claisen condensation, if the substituted acetate, $H—CR_2COOR$, is not readily available, it is easy to introduce the alkyl groups on the α-carbon atoms of an acetoacetate ester.

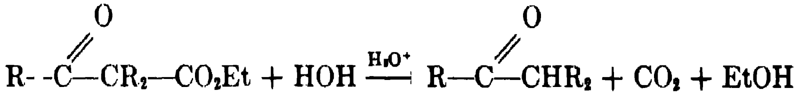


$$R{-}\overset{\overset{O}{\|}}{C}{-}\underset{R'-X}{\overset{\overset{B^-}{H}}{C}}H{-}CO_2Et \rightarrow R{-}\overset{\overset{O}{\|}}{C}{-}\underset{R'}{C}H{-}CO_2Et + BH + X^-$$

A second alkyl group may be substituted for the other α-hydrogen atom in the same fashion.

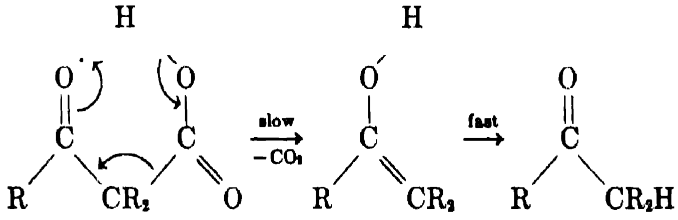
a. Acetoacetic ester synthesis. Upon hydrolysis, the acetoacetate esters yield ketones or acids, depending upon the conditions of hydrolysis.

Ketone formation: In acid or dilute alkali, preferably acid, acetoacetic esters hydrolyze to produce ketones.

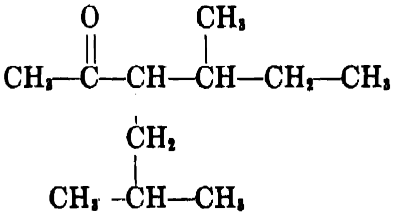


$$R{-}\overset{O}{\overset{/\!/}{C}}{-}CR_2{-}CO_2Et + HOH \xrightarrow{H_3O^+} R{-}\overset{O}{\overset{/\!/}{C}}{-}CHR_2 + CO_2 + EtOH$$

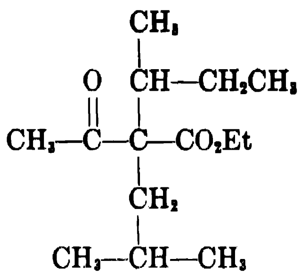
The first step in the reaction is a simple hydrolysis of the ester group to give the acetoacetic acid, but when two COOH groups or a C=O and a COOH group are attached to the same carbon atom, the compound readily loses carbon dioxide. Thus, the acetoacetic acid loses CO_2 during the hydrolysis to yield the ketone.



Thus, quite a variety of ketones may be prepared merely by varying the structures of the R's, and this does not require extremely uncommon compounds. For example, to make the unusual ketone,



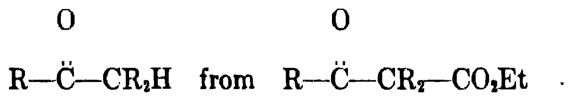
only very common compounds are required. In this case, the acetoacetic ester that would be used is



$$CH_3-\overset{\overset{O}{\|}}{C}-\underset{\underset{\underset{CH_3-CH-CH_3}{|}}{\underset{CH_2}{|}}}{\overset{\overset{\overset{CH_3}{|}}{CH-CH_2CH_3}}{\overset{|}{C}}}-CO_2Et$$

in which the α-alkyl groups are familiar *sec*-butyl and isobutyl groups. The ester, then, can be made from ethyl acetoacetate by substituting the *sec*-butyl and isobutyl groups on the α-positions one at a time, using the respective alkyl bromides and potassium ethoxide catalyst. Of course, the acetoacetate is commercially available, but as a laboratory exercise, it can be prepared from ethyl acetate by the Claisen condensation.

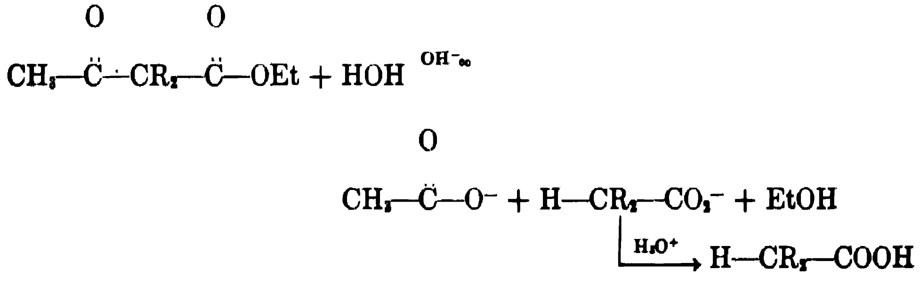
To prepare a complex ketone by this acetoacetic ester synthesis, write down the structure of the desired ketone. One carbon-attached group will be part of the acyl group of the acetoacetic ester, and the other carbon-attached group will have the structure —CR_2H, derived from the α-carbon of the ester.



$$R-\overset{\overset{O}{\|}}{C}-CR_2H \quad \text{from} \quad R-\overset{\overset{O}{\|}}{C}-CR_2-CO_2Et$$

The α-hydrogen of the ketone comes from the decarboxylation step in the hydrolysis.

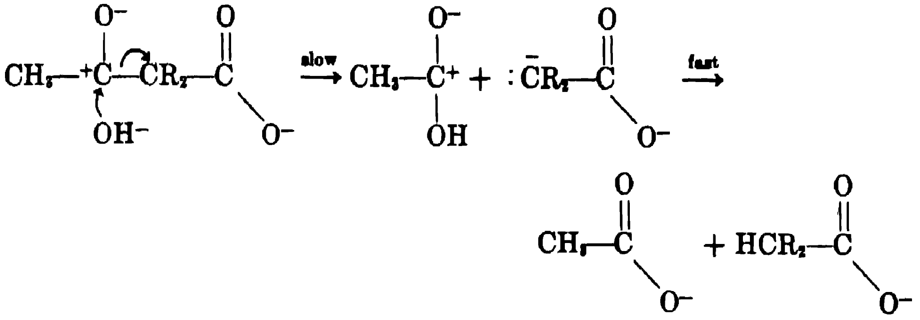
Acid formation: Acids and simple esters cannot be alkylated to give $H-CR_2-COOH$, but such acids can be produced by the hydrolysis of the appropriate acetoacetic esters. For this purpose, acetylacetates are used and the hydrolysis is carried out in strongly alkaline conditions.



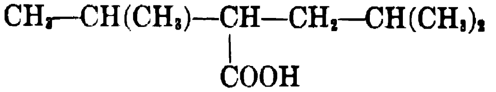
$$CH_3-\overset{\overset{O}{\|}}{C}-CR_2-\overset{\overset{O}{\|}}{C}-OEt + HOH \quad {}^{OH^{-}_{\infty}}$$

$$CH_3-\overset{\overset{O}{\|}}{C}-O^- + H-CR_2-CO_2^- + EtOH \xrightarrow{H_3O^+} H-CR_2-COOH$$

Since the acetic acid is water soluble, and the substituted acetic acid probably will not be, the two are easily separated. Otherwise they would have to be fractionated. In this reaction the initial step again is probably a simple hydrolysis of the ester group, but the salt suffers decarboxylation only very slowly. Instead, the acyl-α-carbon bond undergoes cleavage.

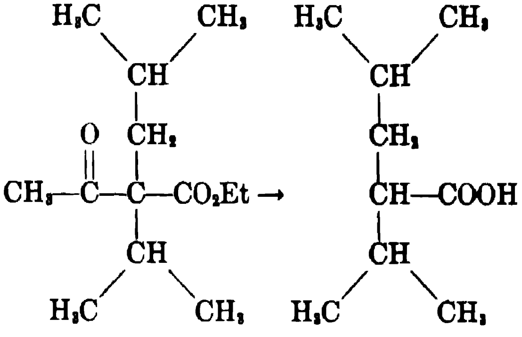


For a complex acid, therefore, if one can pick out the structure $\mathrm{H{-}\overset{|}{\underset{|}{C}}{-}COOH}$, then the acid can be prepared by the acetoacetic acid synthesis wherein whatever appears outside the box must be attached to the α-carbon atom of the acetoacetate ester. For illustration, the acetoacetate required for the preparation of

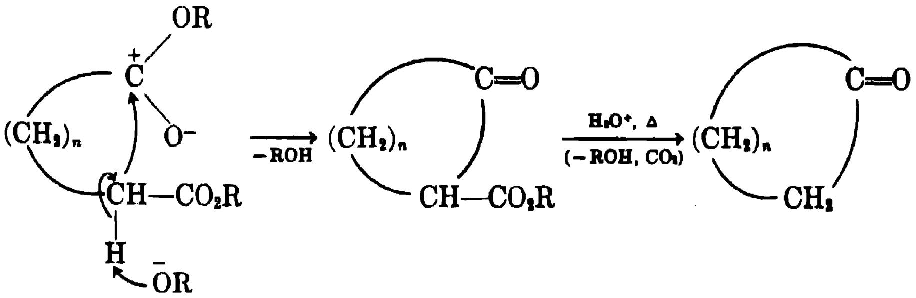


$$\mathrm{CH_3{-}CH(CH_3){-}\underset{\displaystyle COOH}{\underset{|}{C}H}{-}CH_2{-}CH(CH_3)_2}$$

is ethyl α-isopropyl-α-isobutyl-acetoacetate, for in the desired acid, the isopropyl and isobutyl groups are attached to the $\mathrm{H{-}\overset{|}{\underset{|}{C}}{-}COOH}$ group.



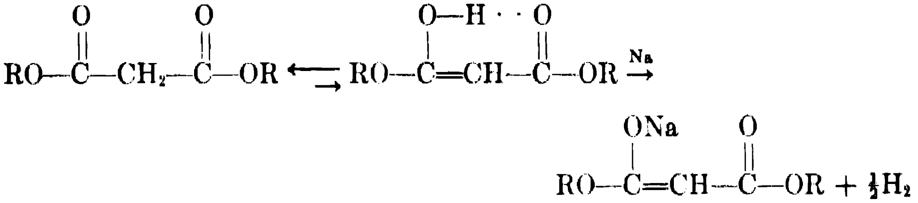
The Claisen condensation will take place intramolecularly, too, in which case it is called the *Dieckmann condensation:*



This reaction provides another way of making alicyclic compounds. Five- and six-membered rings are favored in this condensation and the reaction is preferred over the pyrolysis of the corresponding salts (cf. Section 5.2).

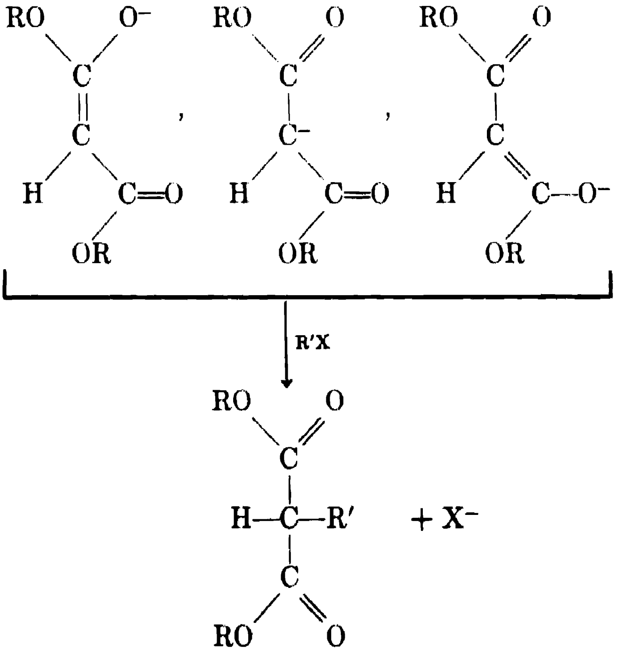
15.6 MALONIC ESTER SYNTHESIS

Malonic esters may be used also for the preparation of substituted acetic acids. Malonic esters may enolize, too, but as shown in Table 15.3, their enol contents are low. When reacted with sodium metal or a strong base, the equilibrium shifts to the enol side and the entire quantity of ester thereby reacts to form a salt.

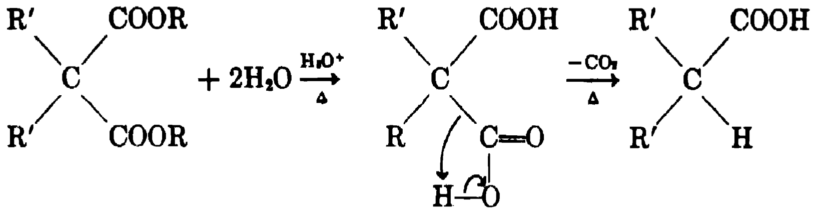


$$RO{-}\overset{\overset{O}{\|}}{C}{-}CH_2{-}\overset{\overset{O}{\|}}{C}{-}OR \rightleftarrows RO{-}\overset{\overset{O-H\cdot\cdot}{|}}{C}{=}CH{-}\overset{\overset{O}{\|}}{C}{-}OR \xrightarrow{Na} RO{-}\overset{\overset{ONa}{|}}{C}{=}CH{-}\overset{\overset{O}{\|}}{C}{-}OR + \tfrac{1}{2}H_2$$

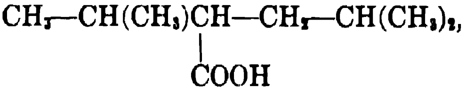
The ion is a resonance hybrid, and reacts as a nucleophilic reagent with alkyl halides.



Malonic esters readily undergo α-halogenation, hence α-alkylmalonates or α-halogenomalonates may be produced. If desired, the second α-hydrogen may also be replaced by either an alkyl group or a halogen atom through the same sequence of reactions. The substituted esters may then be hydrolyzed and decarboxylated to yield substituted acetic acids.

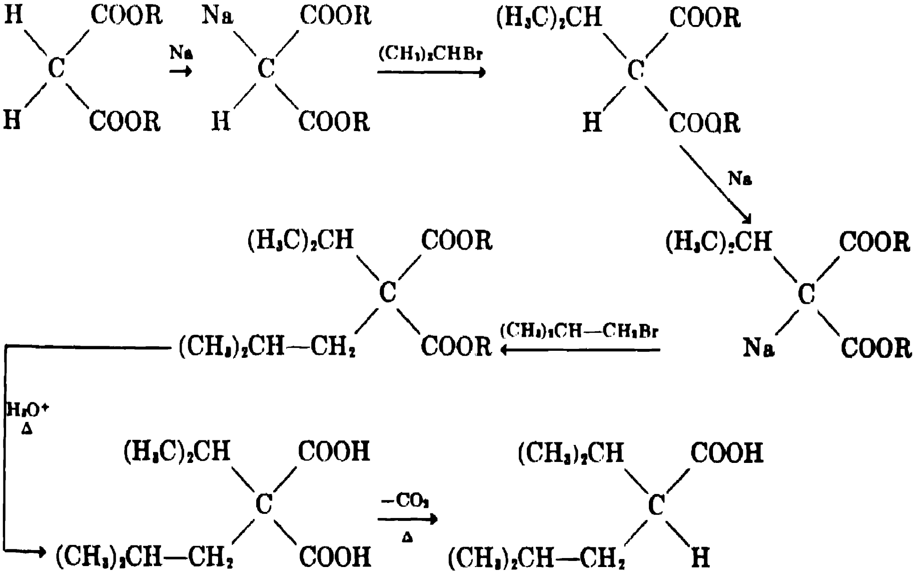


For example, 2,5-dimethyl-3-carboxy-hexane,



$$\mathrm{CH_3{-}CH(CH_3)\underset{\substack{|\\ \mathrm{COOH}}}{CH}{-}CH_2{-}CH(CH_3)_2,}$$

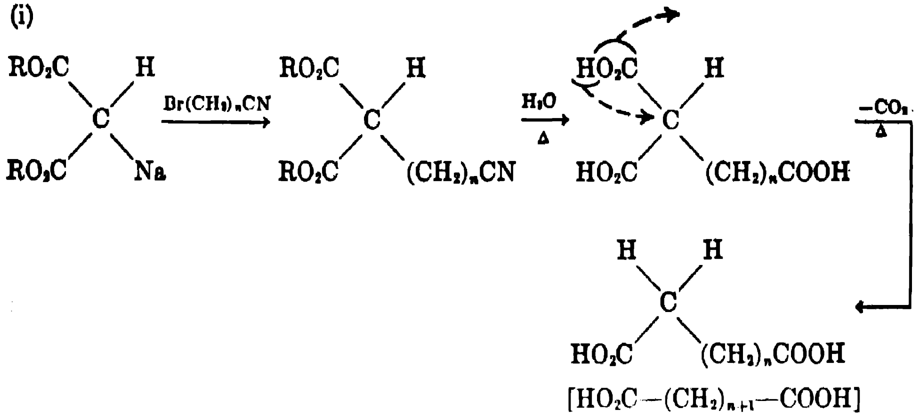
may be prepared from diethyl malonate. As was done for the acetoacetic ester synthesis, pick out $\boxed{\mathrm{H{-}\overset{|}{\underset{|}{C}}{-}COOH}}$ in the structure of the desired acid and what extends out of the box will be the R groups on the α-carbon atoms of the malonic ester. In this case they are the isopropyl and isobutyl groups. Introduce these two groups one at a time into the malonic ester with the use of sodium metal. The sequence of reactions would be as follows. For simplicity the enolization steps and side products are omitted.



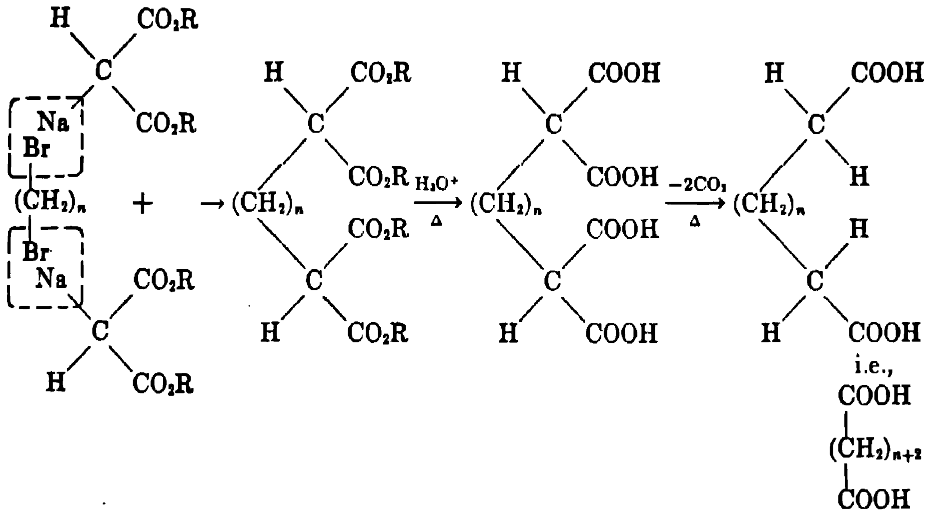
i-Propyl-*i*-butylacetic acid
or
2,3-dimethyl-3-carboxyhexane

Halogenated acids, R—CHX—COOH, are useful for conversion into the corresponding amino acids, R—CH(NH$_2$)—COOH, which are needed in biochemical studies. The malonic ester synthesis also provides methods of preparing alkanedicarboxylic acids.

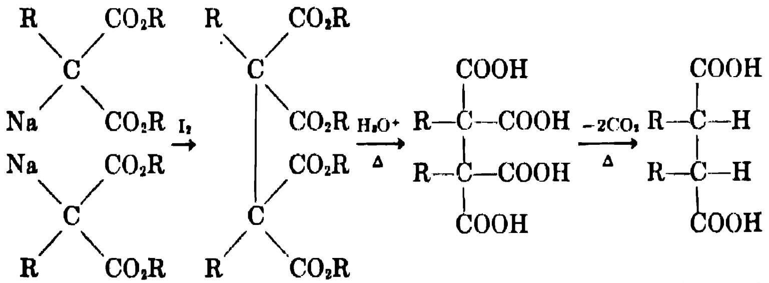
(i)



(ii)



(iii) Substituted succinic acids:



α,α′-Dialkylsuccinic acid

Thus there are many useful applications of the malonic ester synthesis for preparing substituted acids and compounds derivable therefrom.

The malonic ester and acetoacetic ester syntheses produce only dialkylacetic acids. The methods of producing carboxylic acids (e.g., carbonation believe foam indicates efficacy); and (4) other minor additives such as bleaches. Frequently, the bleaches have a white fluorescence to make white clothes look "brighter than white."

A considerable portion of an alkylbenzene sulfonate-based detergent, which accounts for 75 per cent of all household detergents, is not decomposed by sewage treatment plants, and this undegraded detergent, together with other organic substances, produces a pollution and foam problem in our water supply. Although it has been shown that detergents comprise no more than 10 per cent of the organic residue from a sewage treatment plant, detergent manufacturers have had to produce biodegradable detergents. For the present, the alkylbenzene sulfonates are only about 25 per cent biodegradable, whereas the fatty alcohol sulfonates are completely biodegradable.

15.9 ESTERS OF INORGANIC ACIDS

a. Nomenclature and preparation. The esters of inorganic acids are named as alkoxyl derivatives of the inorganic element, or as alkyl replacements of the corresponding salts. For example, $(C_2H_5O)_3P$ is ethyl phosphite, $(C_2H_5O)_3PO$ is ethyl phosphate, $(C_2H_5O)_2SO$ is ethyl sulfite, and $C_2H_5OSO_2H$ is ethyl hydrogen sulfite.

These esters are produced by reactions similar to those used in the preparation of esters of carboxylic acids. Thus, alcohols are reacted with inorganic acids or their acid chlorides. Usually, nitrites, nitrates, sulfates, and borates are prepared from the respective acids (reactions 8 to 12), and phosphites, phosphates, sulfites, and silicates are prepared from the acid chlorides (reactions 13 to 17). In the latter case, a base is added to avoid the accumulation of hydrogen chloride. See list of reactions in Table 15.7. In reactions (13) and (14) notice that phosphorus trichloride may react with alcohols in one of two different ways. Reaction (13) tends to be favored at low temperatures and with primary alcohols; (14), which was used for a method of preparing alkyl halides (see Section 9.2), occurs predominantly with tertiary alcohols. Other inorganic acid halides behave similarly, and the relative proportions of reactions (13) or (14) depend on the conditions and the reactants.

b. Properties of esters of inorganic acids. Such esters have physical and chemical properties much like those of carboxylic acids. They may usually be distilled without decomposition, are soluble in organic solvents, and are insoluble in water. Their tendencies to hydrolyze vary considerably. For example, borates and silicates usually hydrolyze readily at room temperature, but some nitrates hydrolyze slowly at elevated temperatures. In boiling water, the first methyl group of methyl sulfate is hydrolyzed off in a few minutes, but only a fraction of the second methyl group is removed after several hours.

c. Uses of esters of inorganic acids. Most of these esters have marked physiological activities. Nitrites relax the smooth muscles of the body and

TABLE 15.7. PREPARATION OF ESTERS OF INORGANIC ACIDS

$$\mathrm{ROH + HONO \rightarrow HOH + \underset{\substack{\text{An alkyl}\\ \text{nitrite}}}{RONO}} \tag{8}$$

$$\mathrm{ROH + HONO_2 \rightarrow HOH + \underset{\substack{\text{An alkyl}\\ \text{nitrate}}}{RONO_2}} \tag{9}$$

$$\mathrm{ROH + HOSO_2OH \rightarrow HOH + \underset{\substack{\text{An alkyl}\\ \text{hydrogen}\\ \text{sulfate}}}{ROSO_2OH}} \tag{10}$$

$$\mathrm{2ROH + (HO)_2SO_2 \rightarrow HOH + \underset{\substack{\text{An alkyl}\\ \text{sulfate}}}{(RO)_2SO_2}} \tag{11}$$

$$\mathrm{3ROH + B(OH)_3 \rightarrow 3HOH + \underset{\substack{\text{An alkyl}\\ \text{borate or}\\ \text{trialkoxyl}\\ \text{borane}}}{(RO)_3B}} \tag{12}$$

$$\mathrm{3ROH + PCl_3 \rightarrow 3HCl + \underset{\substack{\text{An alkyl}\\ \text{phosphite}}}{P(OR)_3}} \tag{13}$$

$$\mathrm{3ROH + PCl_3 \rightarrow 3RCl + \underset{\substack{\text{Phosphorus}\\ \text{acid}}}{P(OH)_3}} \tag{14}$$

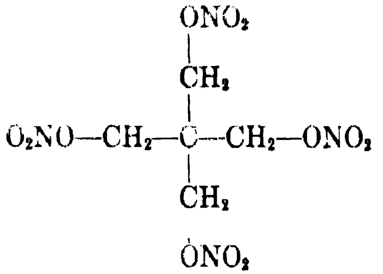
$$\mathrm{3ROH + POCl_3 \xrightarrow{\text{pyridine}} 3HCl{:}pyridine + \underset{\substack{\text{An alkyl}\\ \text{phosphate}}}{(RO)_3PO}} \tag{15}$$

$$\mathrm{2ROH + SOCl_2 \xrightarrow{\text{pyridine}} 2HCl{:}pyridine + \underset{\substack{\text{An alkyl}\\ \text{sulfite}}}{SO(OR)_2}} \tag{16}$$

$$\mathrm{3ROH + SiCl_4 \rightarrow 4HCl + \underset{\substack{\text{Tetra-}\\ \text{alkoxyl-}\\ \text{silane}}}{Si(OR)_4}} \tag{17}$$

rapidly lower blood pressures; sulfates are highly toxic; and silicates affect the eyes.

Many nitrates decompose explosively, and of course, the well-known explosive, nitroglycerin (page 289) is a triester of glycerol. The solid nitrate ester pentaerythritol tetranitrate (PETN) is used extensively in grenades.



$$O_2NO—CH_2—\underset{\underset{ONO_2}{|}}{\underset{CH_2}{|}}{\overset{\overset{ONO_2}{|}}{\overset{CH_2}{|}}{C}}—CH_2—ONO_2$$

PETN

The monoalkyl and dialkyl acid phosphates are used as acid catalysts in the plastics industry, and serve as intermediates or ingredients in the manufacture of flame-proofing agents, rust preventives, antistatic agents, and oil additives. Phosphate esters are used extensively as hydraulic fluids and high-temperature lubricants.

STUDY EXERCISES

1. Give equations for three general methods of preparing esters of carboxylic acids from alcohols.

2. If dithioacetic acid, CH_3CSSH, were reacted with ethanol, what would be the products?

3. What type of soap would be used for (a) toilet soap, (b) for making axle grease, (c) as an antioxidant?

4. Write equations to express the reactions of methyl butanoate with (a) $NaOH_{aq.}$, (b) ammonia, (c) bromine, (d) excess C_2H_5MgBr, (e) $NaOC_2H_5$, (f) $LiAlH_4$.

5. Acetic acid, *n*-propyl alcohol, and methyl formate all have molecular weights of 60. Predict the relative order of their boiling points and state the basis for your prediction.

6. What is the reaction of a soap solution, assumed to be sodium stearate, with (a) copper sulfate solution, (b) "hard water," (c) hydrochloric acid?

7. Write the structural formula of methyl 3-heptynoate.

8. Write a general equation for the preparation of (a) a borate ester, (b) a phosphate ester, (c) a sulfate ester.

9. Starting with $Br—(CH_2)_6—Br$, give two routes for preparing cyclohexanone which involve different methods of closing the ring.

TEST QUESTIONS, Set 15

1. If soap costs 10 cents per pound, how much would it cost to soften 8 liters of a 2% solution of $CaCl_2$? Assume the soap to be sodium stearate, that all of the calcium ions can be removed, and that the specific gravity of the solution is 1.0.

2. Starting with ethyl acetoacetate, indicate the sequence of laboratory reactions one could use to prepare (a) methylisopropyl ketone, (b) methylethylacetic acid, (c) 3-carboxypentane.

3. With ethyl alcohol as the only source of organic compounds, show how one could make use of the acetoacetic ester synthesis to prepare 3-isopropyl-2-heptanone.

4. How could hydroxyacetic acid be prepared from formaldehyde?

5. How could one distinguish by qualitative test-tube experiments (a) ethyl α-methylacetoacetate from ethyl α,α-dimethylacetoacetate, (b) a mineral oil from a vegetable oil?

6. What weight of *substituted* ethyl acetoacetate would be required to produce 71 g of 3-ethyl-4-methyl-2-hexanone if the over-all yield is 50 %?

7. In the reaction of acetic acid with ethyl alcohol, the equilibrium constant is 4. If 2 moles of acetic acid are reacted with 3 moles of ethyl alcohol, how many moles of ethyl acetate are present at equilibrium?

8. By making use of the malonic ester synthesis, indicate the sequence of reactions one could use to prepare the following compounds:

(a) α-methylbutyric acid from diethyl malonate
(b) 2-cyclohexyl-3-methyl-2-pentenoic acid from diethyl malonate
(c) α-chloroadipic acid from diethyl malonate
(d) glutaric acid and adipic acid, each from diethyl malonate
(e) α-benzylvaleric acid from ethyl acetoacetate
(f) isopropyl-*n*-propylacetic acid, with ethyl alcohol as the only source of organic chemicals.

9. What weight of alkyl bromide would be required in the preparation of 51 g of β-methylbutyric acid from diethyl malonate if each step of the reaction gives only an 80% yield?

10. How could one demonstrate that acetoacetic esters are tautomeric?

11. Does 2,5-hexanedione have a larger or smaller enol content than 2,4-hexanedione?

12. How could one distinguish by qualitative test-tube experiments (a) ethyl acetoacetate from diethyl malonate; (b) ethyl α,α-dimethylacetoacetate from methyl butyrylacetate; (c) tristearin from triolein?

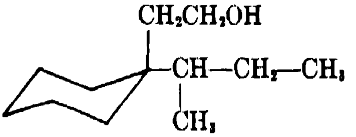
13. Twelve and a half grams of a fat, molecular weight 834, are hydrolyzed in excess alkali, the reaction mixture acidified, and the organic acid isolated. Assuming an 80% yield, what volume of 1 *N* NaOH would be required to neutralize the organic acid?

14. If one has 16 g of diethyl malonate and 15.6 g of ethyl iodide, how much butyric acid could be made by the malonic ester synthesis if the over-all per cent yield is 70%?

15. Write equations for three methods of preparing hydroxyacetic acid starting with formaldehyde in one method, with acetic acid in the second case, and with diethyl malonate in the third preparation.

16. Predict the relative rates of reaction of acetic acid with *n*-, iso-, and *tert*-butyl alcohols, and of ethyl alcohol with *n*-butyric, isobutyric, and trimethylacetic acids.

17. Starting with diethyl α,ω-heptanedioate, what series of reactions would you use in the laboratory to synthesize the following structure?



18. Give the series of reactions that could be used to prepare cycloheptanecarboxylic acid making use of hexamethylene bromide in the malonic ester synthesis. This is an example of Perkin's method of synthesizing alicyclics, and it is useful for rings up to seven carbon atoms.

19. Predict the product in the oxidation of acetophenone with CF_3CO_3H.

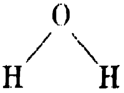
20. Starting with cyclohexane carboxylic acid and bromocycloheptane, and with common commercial substances available, how would you synthesize in the laboratory:

$$C_6H_{11}\text{—}\underset{\displaystyle C_7H_{13}}{\underset{|}{CH}}\text{—}CH_2\text{—}CO_2C_2H_5$$

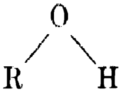
16

Nitrogen Compounds

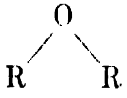
Several of the classes of compounds studied so far have been regarded as derivatives of water in which one or both hydrogen atoms of water have been replaced by alkyl or acyl groups.



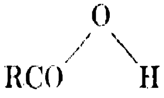
Water



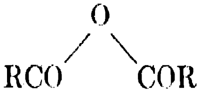
Alcohol



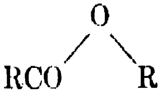
Ether



Acid

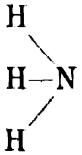


Anhydride

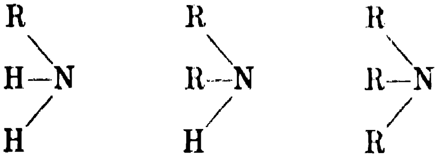


Ester

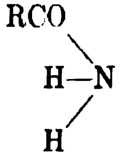
Among the nitrogen compounds to be discussed now, several types may be considered as analogous derivatives of ammonia with 1, 2, or 3 hydrogen atoms replaced by alkyl or acyl groups.



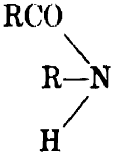
Ammonia



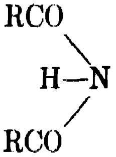
Amines



Amide



N-alkyl amide



Imide

There are other nitrogenous compounds, too, such as

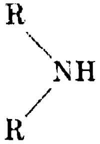
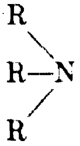
$R_2C{=}NH$	Imine	$RCONHNH_2$	Hydrazide
$RC(NH)NH_2$	Amidine	$R_2C{=}NOH$	Oxime
$RC(NH)OR$	Imido ester	$R_2N{-}NO$	N-nitrosoamine

$R—NO_2$	nitro compound
$R—ONO_2$	nitrate
$R—ONO$	nitrite

as well as amino acids and proteins. Space does not permit a separate discussion of each of these classes of compounds; therefore some will be discussed and others just mentioned throughout this book.

16.1 AMINES

Amines are alkyl derivatives of ammonia, and they fall into three categories:

Primary amines	$R—NH_2$
Secondary amines	
Tertiary amines	

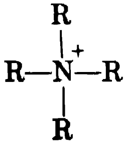
Primary amines are those containing one carbon-attached group in place of a hydrogen atom of ammonia; therefore they also have an NH_2 group. Secondary amines contain two simple carbon-attached groups, having a free NH group; and tertiary amines have all three ammonia hydrogen atoms replaced by carbon-attached groups.

When one or more of the carbon-attached groups is an aromatic ring, the amine is regarded as an aromatic amine:

Primary	*Secondary*	*Tertiary*
$\phi—NH_2$	ϕ_2NH	ϕ_3N
	$\phi—NHR$	ϕ_2NR
		$\phi—NR_2$

Note that $(CH_3)_3C—OH$ is a tertiary alcohol but $(CH_3)_3C—NH_2$ is a primary amine, because the amines are classified on the basis of the number of alkyl groups (substituents) which have replaced H atoms of NH_3.

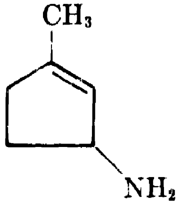
Just as ammonia may form ammonium salts by sharing its lone electron pair with an acid, a tertiary amino-nitrogen atom may share its lone electron pair with a carbonium ion to form a quaternary ammonium ion.



$$R_4N^+$$

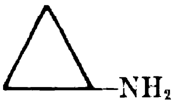
Each group is joined to nitrogen by a covalent bond. Being an ion, it forms salts with anions, as does the ammonium ion.

a. Nomenclature. The I.U.C. system of naming aliphatic amines replaces the -*e* ending in the name of the corresponding hydrocarbon by -*amine*. For example, $CH_3CH_2CHNH_2CH_3$ is 2-butanamine. On the other hand, in more complex structures it is convenient to regard the amino group as a substituent.

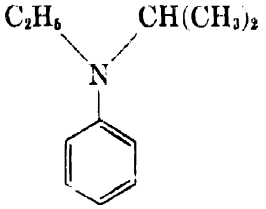


3-Amino-1-methylcyclopentane

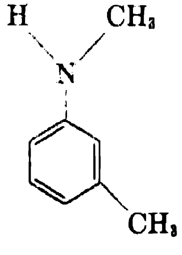
The common names of amines are obtained by giving the name of the alkyl groups and adding the suffix, amine. Aromatic amines are named as derivatives of the parent amine. Some examples follow:



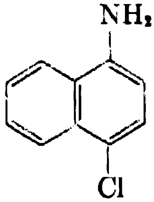
Cyclopropylamine



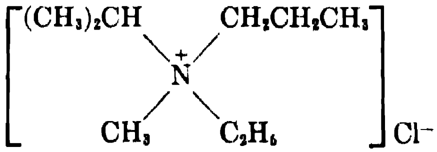
Phenylethylisopropylamine
or
N-ethyl-N-isopropylaniline



N-methyl-*m*-toluidine



4-Chloro-1-naphthylamine



Ethylmethylisopropyl-*n*-propylammonium chloride

$(HOCH_2CH_2)_2NH$ Bis-β-ethanolamine

$H_2N—(CH_2)_n—NH_2$ Polymethylenediamine

Hexamethylenediamine (1,6-diaminohexane) is used as a monomer in the preparation of nylon (page 586). *Putrescine*, tetramethylenediamine, and *cadaverine*, pentamethylenediamine, are formed when meat and fish decay. As the names imply, their odors are obnoxious. They are not highly toxic themselves but belong to a group of poisonous substances called *ptomaines*, which are nitrogenous compounds formed in the decomposition of proteins by bacteria.

b. Preparation. In the alkylation of ammonia with alkyl halides, an alkylammonium salt is first produced, which reacts with ammonia to form NH_4X plus a primary amine:

$$H_3N: + R{-}X \rightleftharpoons [H_3N \cdots R \cdots X] \rightarrow RNH_3X \xrightarrow{NH_3} RNH_2 + NH_4X$$

This is a displacement reaction in which the more basic amino group replaces the halogen atom. However, some of the resulting primary amines can react in the same way with some of the alkyl halide which has not yet reacted, to produce a secondary amine.

$$R\ddot{N}H_2 + R{-}X \xrightarrow{NH_3} R_2NH + NH_4X$$

The secondary amine can also react with unreacted alkyl halide to yield a tertiary amine, which in turn may react with alkyl halide to give a quaternary ammonium salt.

$$\begin{aligned} R_2NH &+ R{-}X \xrightarrow{NH_3} R_3N + NH_4X \\ R_3N &+ R{-}X \xrightarrow[\Delta]{} R_4NX \end{aligned}$$

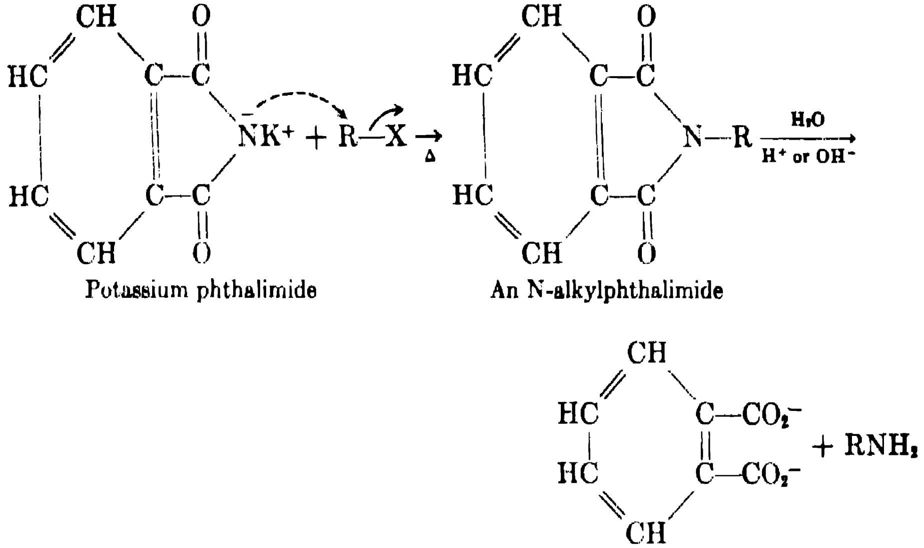
Thus, the reaction produces four products, decreasing in amounts as the degree of alkylation progresses. Although the products may be separated by some form of fractionation, a chemist prefers to use a preparative method which does not require extensive fractionation of the products. For that reason this reaction is not used for the laboratory preparation of primary amines.

Nevertheless, alkylation of ammonia can be used for the industrial production of amines, for then the reaction mixture is easily fractionated and the various products placed in stock for sale when ordered. The methylamines are also produced commercially by a catalytic reaction between ammonia and methanol.

$$CH_3OH + NH_{3\,\text{excess}} \xrightarrow[450^\circ]{Al_2O_3} \begin{Bmatrix} CH_3NH_2 \\ (CH_3)_2NH \\ (CH_3)_3N \end{Bmatrix} + H_2O$$

Preparation of aliphatic primary amines.

Gabriel synthesis.

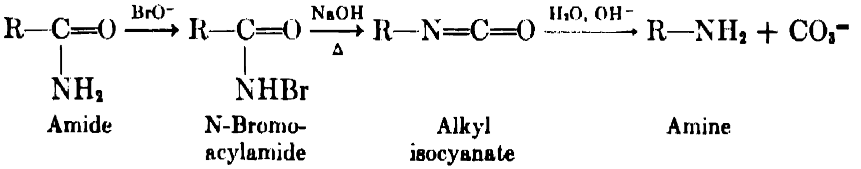


The alkyl halide and potassium phthalimide are warmed in a solvent, dimethylformamide being particularly good, and then the N-alkylphthalimide is hydrolyzed in acid or alkali to yield the amine.

Hofmann reaction. This reaction proceeds by way of two intermediates which may be isolated under certain conditions.

$$RCONH_2 + Br_2 + 4NaOH \rightarrow RNH_2 + Na_2CO_3 + 2NaBr + 2H_2O$$

The first step is the formation of an N-bromoamide through bromination by the hypobromite ion. (Recall that halogens in alkaline solution exist as hypohalite plus halide ions.) The N-bromoamide then undergoes a molecular rearrangement to yield an isocyanate. This suffers hydrolysis to give the amine.



$$\underset{NH_2}{\underset{|}{R-C{=}O}} \xrightarrow{BrO^-} \underset{NHBr}{\underset{|}{R-C{=}O}} \xrightarrow[\Delta]{NaOH} R-N{=}C{=}O \xrightarrow{H_2O,\ OH^-} R-NH_2 + CO_3^{=}$$

Reduction of nitriles, nitroalkanes, or amides.

$RCN \xrightarrow{R.A.} RCH_2NH_2$ R.A. = Na in EtOH, or $LiAlH_4$

$RNO_2 \xrightarrow{R.A.} RNH_2$ R.A. = $LiAlH_4$, or Sn or Zn in HCl

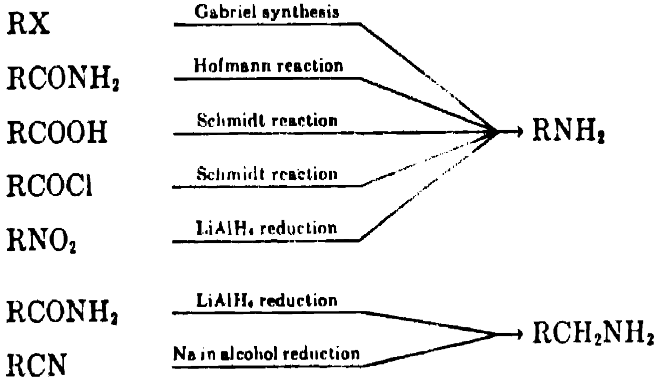
$RCONH_2 \xrightarrow{R.A.} RCH_2NH_2$ R.A. = $LiAlH_4$

In each of these reductions, catalytic hydrogenation may also be used, but often the elementary laboratory is not equipped to do so.

Schmidt reaction. This reaction was discussed in connection with the chemical properties of carboxylic acids (page 347).

$$\left.\begin{array}{c}\mathrm{RCOOH}\\ \mathrm{or}\\ \mathrm{RCOCl}\end{array}\right\} + \mathrm{HN_3} \rightarrow \mathrm{RNH_2} + \mathrm{CO_2} + \mathrm{N_2}$$

It can be seen, therefore, that aliphatic primary amines may be prepared from several different classes of compounds.



Preparation of aromatic primary amines. Primary aromatic amines are usually prepared by the reduction of the corresponding nitrobenzenes. The most common procedure is to use a metal in acid solution.

$$\phi\text{—}\mathrm{NO_2} + \mathrm{M} \xrightarrow{\mathrm{H_3O^+}} \phi\text{—}\mathrm{NH_3^+} + \mathrm{M^{n+}} \qquad \mathrm{M} = \mathrm{Zn, Sn, Fe, or\ SnCl_2}$$

Occasionally, catalytic hydrogenation or electrolytic reductions are used. Primary amines may be prepared also by ammonolysis of aryl halides; although the reaction is not convenient to carry out in the elementary laboratory.

$$\phi\text{—}\mathrm{X} + 2\mathrm{NH_3} \xrightarrow[200^\circ]{\mathrm{Cu_2O}} \phi\text{—}\mathrm{NH_2} + \mathrm{NH_4X}$$

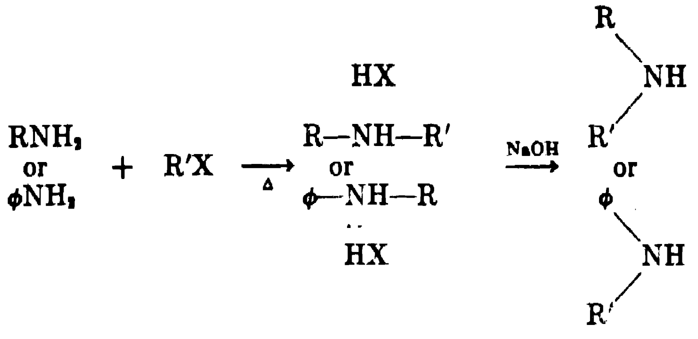
Preparation of secondary and tertiary amines.

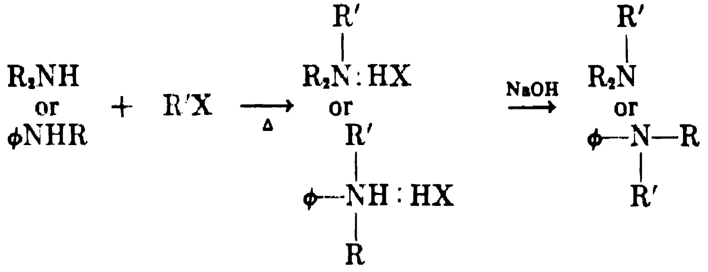
Alkylation of lower amines.[1]

---

[1] In addition to the methods given here, tertiary amines of the type $\mathrm{RN(CH_3)_2}$ can be prepared conveniently by the action of formic acid plus formaldehyde on primary amines (Cf. A. C. Cope, *et al.*, *J. Am. Chem. Soc.*, **77**, 1628 (1955).

$$\mathrm{RNH_2} + \mathrm{HCO_2H} + \mathrm{H_2CO} \xrightarrow[\Delta]{} \mathrm{R\text{—}N(CH_3)_2}$$

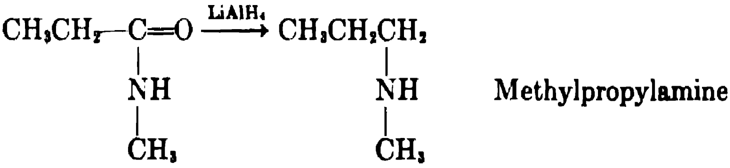




$$\begin{matrix} R_2NH \\ \text{or} \\ \phi NHR \end{matrix} + R'X \xrightarrow[\Delta]{} \begin{matrix} R_2\overset{R'}{\underset{}{N}}:HX \\ \text{or} \\ \phi\text{—}\overset{R'}{\underset{R}{N}}H:HX \end{matrix} \xrightarrow{NaOH} \begin{matrix} R_2\overset{R'}{N} \\ \text{or} \\ \phi\text{—}\underset{R'}{N}\text{—}R \end{matrix}$$

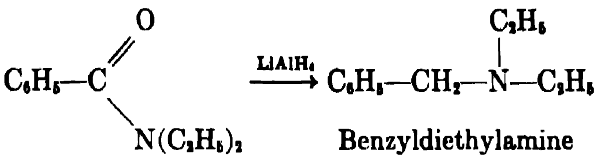
In the preparation of the secondary amine, some tertiary amine is also produced and can be removed by fractionation, or better, by the Hinsberg method (see page 412). Similarly, in the preparation of the tertiary amine, some quaternary ammonium salt is produced, which may easily be removed owing to its water solubility.

Reduction of amides. N-Alkyl amides of the types R—CONHR and R—CONR$_2$ may be reduced with LiAlH$_4$ to secondary and tertiary amines, respectively.



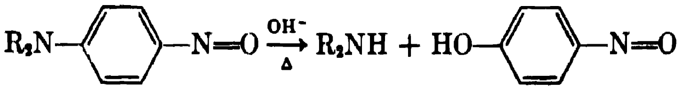
$$CH_3CH_2\text{—}\underset{\underset{CH_3}{|}}{\underset{NH}{\underset{|}{C}}}=O \xrightarrow{LiAlH_4} CH_3CH_2\underset{\underset{CH_3}{|}}{\underset{NH}{\underset{|}{CH_2}}}$$

Methylpropylamine



Benzyldiethylamine

Hydrolysis of nitrosoanilines. Nitroso derivatives of N,N-dialkylanilines hydrolyze in base to yield secondary amines.



Preparation of quaternary ammonium salts. These salts are prepared by gently warming an alkyl halide with a tertiary amine in a solvent like alcohol. The salt precipitates as a clean, usually colorless, crystalline material.

$$R_3N + RX \rightarrow R_4NX$$

In alcoholic KOH or with silver oxide, the salts may be converted to the corresponding hydroxides.

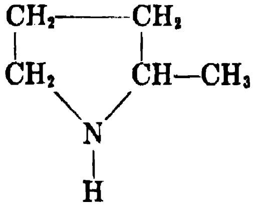
$$R_4NX + KOH_{alc.} \rightarrow R_4NOH + KX$$

The tetraalkylammonium hydroxides are strong bases like sodium hydroxide, and are completely ionized in aqueous solution.

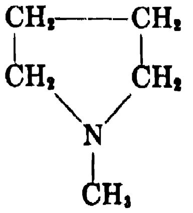
c. Physical properties of amines. (See Table 16.1.) In addition to hydroxylic compounds, amines also form hydrogen bonds. For example, primary and secondary amines form N—H · · · N hydrogen bonds with themselves, which makes them have higher boiling points than isomeric tertiary amines which cannot form the hydrogen bonds.

TABLE 16.1. PHYSICAL CONSTANTS OF SOME AMINES

Name	Melting Point	Boiling Point	K_b
Methylamine	−92	−7.5	4.4×10^{-4}
Dimethylamine	−96	7.5	5.1 "
Trimethylamine	−117	3	0.6 "
Ethylamine	−80	17	4.7 "
Diethylamine	−39	55	9.5 "
Triethylamine	−115	89	5.5 "
n-Propylamine	−83	49	3.8 "
n-Butylamine	−50	78	4.1 "
Cyclohexylamine		134	
Benzylamine		185	0.23 "
Aniline	−6	184	4.2×10^{-10}
N-Methylaniline	−57	196	7.1 "
N,N-Dimethylaniline	3	194	11 "
p-Toluidine	44	200	12 "
p-Anisidine	57	244	15 "
p-Nitroaniline	148	332	0.001 "



2-Methylpyrrolidine
B.p. = 100°



N-Methylpyrrolidine
B.p. = 79°

A good example of intermolecular forces decreasing with diminishing hydrogen bonding is found in the methylhydroxylamines.

Compound	Melting Point	Boiling Point	$\Delta H_{vap.}$ cal/mole
$HONHCH_3$	38.5°	115°	11,880
$HON(CH_3)_2$	17.6	100.6	9,670
CH_3ONH_2	−86.4	48.1	7,710
$CH_3ONH(CH_3)$	−97.0	42.3	7,440
$CH_3ON(CH_3)_2$	−97.2	30.0	6,410

The same trend is found for the melting point, boiling point, and the heat of vaporization. Hydrogen bonds involving OH groups are stronger than those between NH groups, as shown by the big differences when the OH group is methylated.

A hydrogen bridge may also occur between a nitrogen and an oxygen atom. Thus, because of association with water molecules through hydrogen bonds, amines have considerable solubilities in water. The primary amines up to *n*-pentylamine and the secondary amines up to di-(*n*-butyl)-amine are completely miscible with water, whereas even the first tertiary amine (trimethylamine) is only 41 per cent soluble and the higher tertiary amines are practically insoluble in water. Hence, polyhydroxy and polyamino compounds have marked water solubilities as a result of hydrogen bonding with water molecules. Because of this fact, they can serve as nonionic detergents (page 390). The solubilities of amines in ether are in direct contrast to those in water. As the hydrocarbon to amine group ratio decreases, the solubility in ether decreases and the water solubility increases. For example, ethylenediamine is practically insoluble in ether, but the higher polymethylenediamines are soluble.

Amines are the typical organic bases. Toward protonic acids, their basicities are of the same order of magnitude as that of ammonia, and their behavior in water resembles that of ammonia.

Ammonia

$$NH_3 + HOH \rightleftarrows (NH_4OH) \rightleftarrows NH_4^+ + OH^-$$

$$K_b = \frac{(NH_4^+)(OH^-)}{(NH_3)} \simeq 10^{-5}$$

Amines

$$R_3N + HOH \rightleftarrows (R_3NHOH) \rightleftarrows R_3NH^+ + OH^-$$

$$K_b \quad \frac{(R_3NH)(OH^-)}{(R_3N)} \quad 10^{-5}$$

Thus, ammonia and the amines are weak bases but strong enough to give a basic reaction to litmus paper. To protonic acids, the order of relative base strength is found to be $R_2NH > RNH_2 > R_3N > NH_3$, revealing that the substitution of alkyl groups for hydrogen of ammonia increases the base strength of the nitrogen.[2]

Since hydrogen atoms are more electronegative than alkyl groups, hydrogen atoms pull the shared pairs of electrons away from nitrogen more than do alkyl groups, making the nitrogen of ammonia less willing to share its lone-pair electrons with an acid. Hence, one would expect the amines and ammonia to have base strengths in the order $R_3N > R_2NH > RNH_2 > NH_3$. H. C. Brown and his co-workers have shown, however, that the reference acid is of tremendous importance in determining the relative base strength of two or more amines. For illustration, in accordance with the empirical rule that "stronger base liberates weaker base from its salt," trimethylamine liberates pyridine from its salts with HCl, BH_3, and BF_3, indicating that trimethylamine is the stronger base to these acids.

$$(CH_3)_3N\!: + \underset{\substack{\text{Pyridine}\\ \text{hydrochloride}}}{C_5H_5N\!:\!HCl} \rightarrow (CH_3)_3N\!:\!HCl + C_5H_5N\!:$$

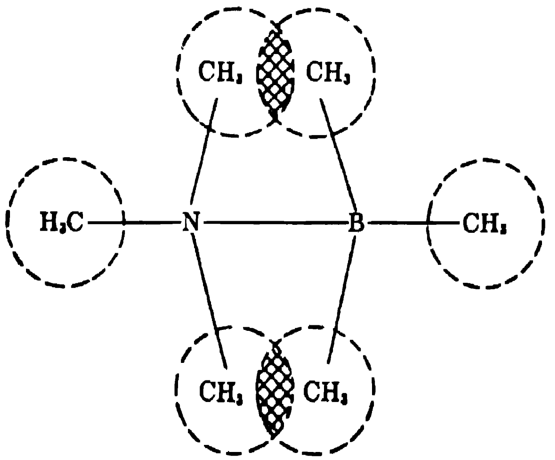
$$(CH_3)_3N\!: + C_5H_5N\!:\!BH_3 \rightarrow (CH_3)_3N\!:\!BH_3 + C_5H_5N\!:$$

$$(CH_3)_3N\!: + C_5H_5N\!:\!BF_3 \rightarrow (CH_3)_3N\!:\!BF_3 + C_5H_5N\!:$$

On the other hand, to $B(CH_3)_3$ pyridine is the stronger base and liberates trimethylamine from the salt.

$$C_5H_5N\!: + (CH_3)_3N\!:\!B(CH_3)_3 \rightarrow C_5H_5N\!:\!B(CH_3)_3 + (CH_3)_3N\!:$$

This reversal in relative base strengths is due to steric hindrance.



Owing to the overcrowding in the salt at the interface of the base-acid, a salt may be so unstable that there is little tendency for it to form, thereby resulting in a low apparent base strength for the amine. In pyridine, the atoms attached to nitrogen are held back out of the front plane of the nitrogen atom and do not interfere with its neutralization.

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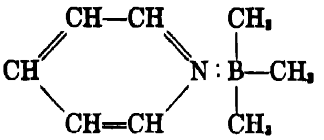
[2] It is noteworthy that the opposite electron-withdrawing effect of many fluorine atoms makes the perfluoroamines such weak bases that they do not form salts with even very strong acids such as $AlCl_3$.



Another illustration of this steric effect upon relative base strengths is found by changing the size of the alkyl groups on nitrogen. Upon increasing the bulkiness of the alkyl groups on the nitrogen of ammonia, the following orders of relative base strengths toward trimethylboron are found.

Alkyl Group	*Relative Base Strength to* $B(CH_3)_3$
CH_3—	$R_2NH > RNH_2 > R_3N > NH_3$
CH_3CH_2—	$R_2NH > RNH_2 > NH_3 > R_3N$
$(CH_3)_2CH$—	$RNH_2 > NH_3 > R_2NH > R_3N$
$(CH_3)_3C$—	$NH_3 > RNH_2 > R_2NH > R_3N$

Thus, as the size of the alkyl group increases, thereby increasing the steric repulsion in the salts, the relative base strengths diminish until finally ammonia is the strongest base. Furthermore, with the increase of the size of the alkyl groups on the acid, the steric hindrance increases even more rapidly, and with tri-*t*-butylboron, the last sequence above occurs even when ethyl groups are on the nitrogen.

Since amines are weak bases, their salts, which are completely ionized in water, hydrolyze just as do ammonium salts.

$$\overset{+}{N}H_4 + 2HOH \rightleftharpoons (NH_4OH) + H_3\overset{+}{O} \qquad R_3\overset{+}{N}H + 2HOH \rightleftharpoons (R_3NHOH) + H_3\overset{+}{O}$$

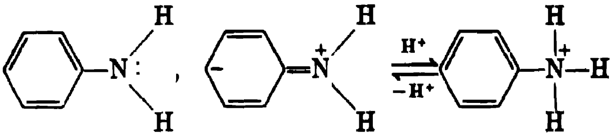
$$K_{\text{hydrolysis}} = \frac{K_w}{K_b} \simeq \frac{10^{-14}}{10^{-5}} \simeq 10^{-9}$$

Accordingly, aqueous solutions of amine salts are just on the acid side of neutrality. This is due to hydrolysis and not to the splitting off of the acid. That is, $R_3N : HCl$ is not acidic because of the HCl in the salt, but is acidic because of the weakness of the base; in other words, it is acidic because the R_3NH^+ ion takes an hydroxide ion from water to liberate a proton. The salts, of course, are insoluble in ether and have very small volatilities.

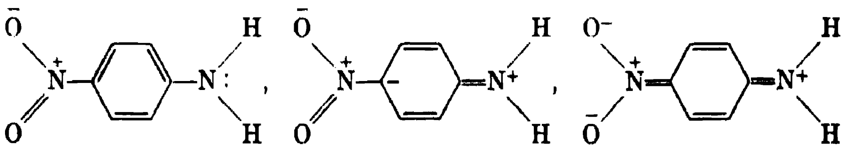
Aromatic amines are much weaker bases than aliphatic amines. For example, the K_b for aniline is about 10^{-10}. As a rule, alkyl groups *increase* the basicity of nitrogen, and aryl groups *decrease* the basicity of nitrogen. This may be seen qualitatively from the following generalization:

Aryl Amines	*Diaryl Amines*	*Triaryl Amines*
$\phi NR_2 > \phi NHR > \phi NH_2$	$\phi_2NR > \phi_2NH$	ϕ_3N
Form salts and dissolve in dilute strong acid	Form salts with conc. strong acids only	Do not form salts

There are several factors which affect the basicity of aryl amines. The chief effects are (1) induction and resonance effects in the free base, (2) steric effects in the free base, and (3) steric effects in the salt. The most important factor is resonance in the base.



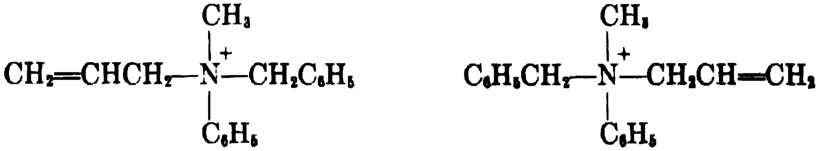
Nitrogen-phenyl group resonance occurs in the aryl amine, but not in the salt. The base is more stable than it would be in the absence of resonance. This shifts the equilibrium to the left. Since this base-weakening resonance does not occur in alkyl amines, they are stronger bases than aryl amines. The more aryl groups attached to the nitrogen, the greater is the amount of resonance and the weaker is the base. Furthermore, groups which will readily accept the negative charge of the ionic structure above, thereby increasing the contribution of the ionic form, decrease the base strength of the nitrogen still further.



Thus, *o*- and *p*-nitroanilines are weaker bases than aniline, as are all substituted anilines with *m*-directing groups in the *ortho* or *para* positions.

Aromatic amines are generally slightly soluble in water and are steam distillable. They are very toxic externally as well as internally.

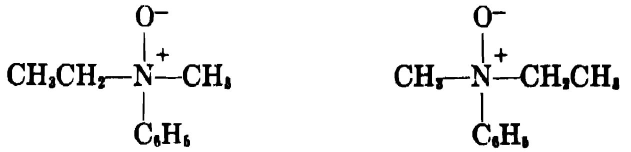
Optical isomerism of quaternary ammonium salts: When there are four different groups attached to a nitrogen atom, there is no plane of symmetry through the molecule and hence optical isomers arise.



$$CH_2{=}CHCH_2{-}\overset{\overset{CH_3}{|}}{\underset{\underset{C_6H_5}{|}}{\overset{+}{N}}}{-}CH_2C_6H_5 \qquad C_6H_5CH_2{-}\overset{\overset{CH_3}{|}}{\underset{\underset{C_6H_5}{|}}{\overset{+}{N}}}{-}CH_2CH{=}CH_2$$

d- and *l*-Allyl-benzyl-methyl-phenylammonium ions
(first resolved in 1899)

Similarly, amine oxides may be asymmetric, resulting in optical isomers.



$$CH_3CH_2{-}\overset{\overset{O^-}{|}}{\underset{\underset{C_6H_5}{|}}{\overset{+}{N}}}{-}CH_3 \qquad CH_3{-}\overset{\overset{O^-}{|}}{\underset{\underset{C_6H_5}{|}}{\overset{+}{N}}}{-}CH_2CH_3$$

d- and *l*-Ethylmethylphenylamine oxide
(first resolved in 1908)

d. Chemical properties of amines.

Reactions with nitrous acid:

ALIPHATIC AMINES

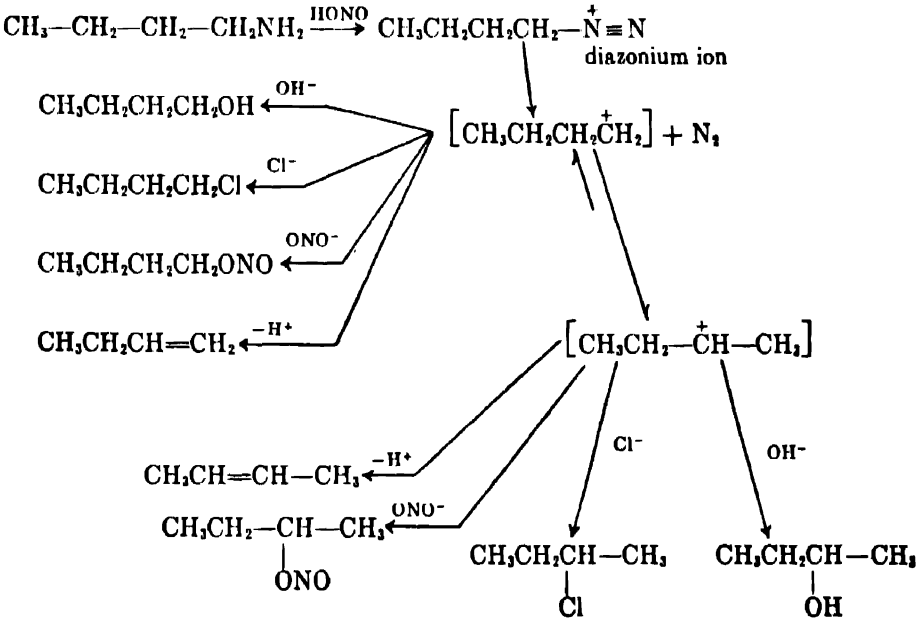
$$RNH_2 + HONO \rightarrow ROH + N_2 + H_2O \qquad (1)$$

$$R_2NH + HONO \rightarrow \underset{\substack{\text{N-Nitrosoamine} \\ \text{(yellow or green,} \\ \text{water-insoluble,} \\ \text{ether-soluble)}}}{R_2N\text{—}NO} + HOH \qquad (2)$$

$$R_3N + HONO \rightarrow \underset{\text{A salt}}{R_3N : HNO_2} \qquad (3)$$

This contrasting behavior of the amines with nitrous acid is occasionally used to differentiate the three classes of amines. Thus, a primary amine liberates a gas (N_2), a secondary amine gives a water-insoluble oil, sometimes yellow in color, and a tertiary amine merely gives a water-soluble salt. Reaction (1) is sometimes used as a method of replacing an NH_2 group by an OH group. The reaction usually gives low yields and several side products, so it is employed as a step in a multistep synthesis only when it is unavoidable.[1]

The primary amine and nitrous acid react to produce a diazonium ion which decomposes to a carbonium ion. The latter may then react to produce an alcohol, alkyl halide, nitrite ester, or olefin, or it may rearrange and then yield the isomeric set of compounds.



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[1] The replacement of NH_2 by OH can be done in a fairly good yield by the series of reactions:

$$RNH_2 \xrightarrow{(R'CO)_2O} RNHCOR' \xrightarrow{HONO} RN(NO)COR' \xrightarrow[\Delta]{-N_2} RO\text{—}COR' \xrightarrow[\Delta]{H_3O^+} ROH$$

This route uses reactions that are simple to carry out, but is more than a short step from the amine to the alcohol (E. H. White, *J. Amer. Chem. Soc.*, **77**, 6011 (1955)).

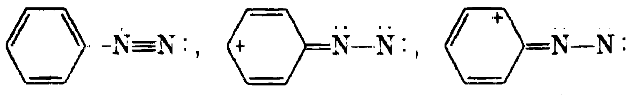
AROMATIC AMINES

In contrast to the aliphatic amines, aromatic amines give relatively stable diazonium ions upon reaction with nitrous acid. This is known as the *diazotization reaction.*

$$\phi\text{—NH}_3^+ + \text{HONO} \xrightarrow{0^\circ} \phi\text{—}\overset{+}{\text{N}}\equiv\text{N} + 2\text{H}_2\text{O}$$

A diazonium
ion

Here is another example of the stabilizing effect of resonance. The aromatic diazonium ion is a resonance hybrid of several forms.



Analogous structures are not possible for aliphatic ions

Nitrous acid is not a stable acid and is not kept in stock. It is prepared when needed by adding hydrochloric or sulfuric acid to a nitrite salt. In this acid medium, the amine is present as the salt. Diazonium ions form soluble salts with some anions and insoluble salts with others, just as some silver salts are water soluble and others are not. Usually, chloride and sulfate diazonium salts are water soluble, and fluoroborates, naphthalenesulfonates, and trifluoroacetates are insoluble. The water-soluble salts ionize and are stable in cold water but react with water when heated. They decompose easily in the dry state. On a commercial scale, these salts must be handled very carefully. They may be linked with zinc chloride to form stable double salts.

The major importance of diazonium salts is their use for preparing many classes of compounds through replacement of the diazonium group:

1. *By OH:*

$$\phi\text{—N}_2^+ + 2\text{H}_2\text{O} \xrightarrow{50\text{–}100^\circ} \phi\text{—OH} + \text{N}_2 + \text{H}_3\text{O}^+$$

This reaction is used for the laboratory preparation of phenols. When the cold diazotization reaction mixture is warmed up, the diazonium ion reacts to form the phenol. In the case of aliphatic amines, the intermediate diazonium ion is unstable and decomposes immediately to form the alcohol.

2. *By I, Cl, Br, CN (Gattermann reaction):*

$$\phi\text{—N}_2^+ + \text{KX} \xrightarrow{\text{Cu}} \phi\text{—X} + \text{K}^+ + \text{N}_2 \qquad \text{X} = \text{I, Br, Cl, CN}$$

The catalyst is not required when X = I. Better yields are usually obtained with cuprous salt, and the reaction is then called the *Sandmeyer reaction.*

$$\phi\text{—N}_2^+ + \text{CuX} \xrightarrow[\Delta]{} \phi\text{—X} + \text{N}_2 + \text{Cu}^+ \qquad \text{X} = \text{Cl, Br, CN}$$

Notice that these reactions provide methods for preparing iodobenzenes and benzonitriles (phenyl cyanides).

3. By F (Schiemann reaction):

$$\phi N_2^+ + BF_4^- \rightarrow \phi N_2BF_4 \xrightarrow[\Delta]{} \phi\text{—}F + N_2 + BF_3$$

This reaction provides a good method of making aryl fluorides. The benzenediazonium fluoroborate salt is usually insoluble in water, and precipitates when the fluoroborate ion is added in the form of fluoroboric acid (HBF_4) or its sodium salt. The diazonium salt is filtered, dried, then heated to decomposition, yielding the fluorobenzene and huge volumes of BF_3 and nitrogen.[4] An alternative modification of this reaction has been to diazotize in fluoroboric acid and decompose the diazonium fluoroborate in aqueous acetone in the presence of cuprous chloride.

4. By NO_2:

$$\phi N_2BF_4 + NO_2^- \xrightarrow{Cu} \phi\text{—}NO_2 + BF_4^- + N_2$$

5. By H (Deamination):

$$\xrightarrow[0\text{–}5^\circ]{H_3PO_2} \phi\text{—}H + N_2 + H_3PO_3$$

$$\phi N_2BF_4 \xrightarrow{NaBH_4} \phi\text{—}H + N_2$$

A variety of reducing agents may be used to reduce the diazonium salt. Hypophosphorous acid and sodium borohydride are two that generally give good yields. Furthermore, the use of D_3PO_2 makes it possible to replace the diazonium group by deuterium, $\phi N_2^+ \rightarrow \phi\text{—}D$.

6. By aryl:

$$\phi\text{—}N_2^+ + \phi'\text{—}H \xrightarrow{\text{base}} \phi\text{—}\phi' + N_2 + H^+ \qquad \text{Base} = \text{NaOH, or AcONa}$$

Sodium acetate is generally a good catalyst. This is the method mentioned in Section 8.3a for making unsymmetrical biphenyls. It is a weak reaction and, if there is a choice, the reaction is carried out so that *m*-directing groups are not in the ϕ' ring. For illustration, if it is desired to prepare *m*-nitro-*p*'-methoxybiphenyl, the best method would be to use *m*-nitrobenzene diazonium ion with anisole.

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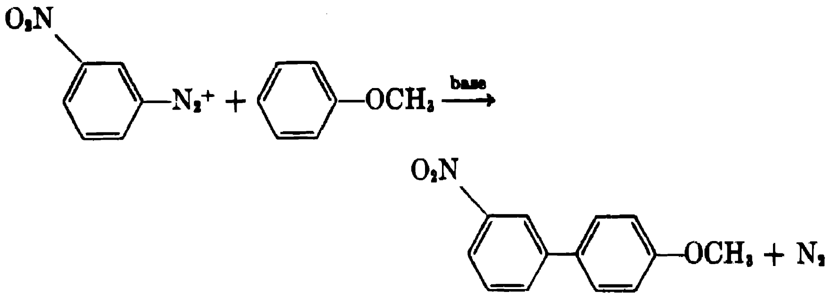
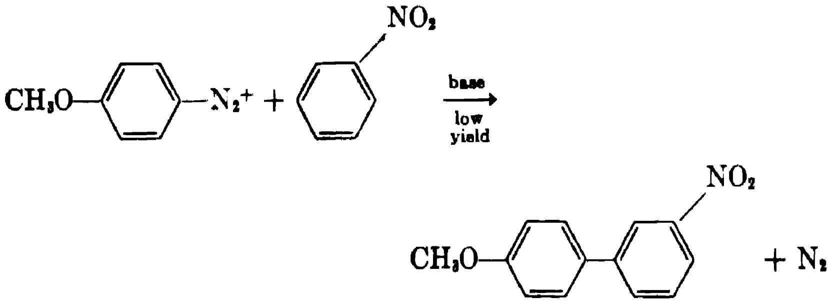
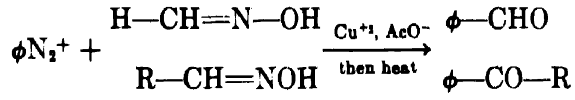
[4] In contrast to this, ϕN_2BCl_4 salts decompose vigorously, sometimes explosively, when heated (Olah and Tolgyesi, *J. Org. Chem.*, **26**, 2053 (1961)). In some cases, hexafluorophosphoric acid, HPF_6, is better than fluoroboric acid. For instance, anthranilic acid gives 19 and 78 per cent yields, respectively, with HBF_4 and HPF_6 (K. G. Rutherford, *et al.*, *J. Org. Chem.*, **26**, 5149 (1961)).



The alternative coupling would give a low yield.



7. *By acyl:*

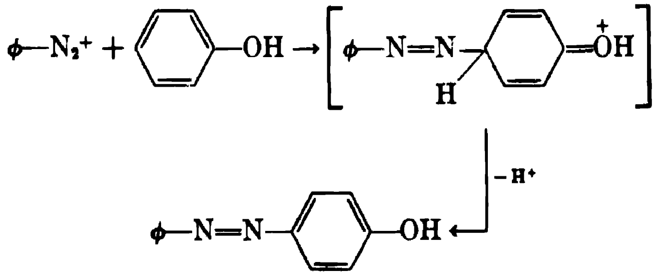


$$\phi N_2^+ + \begin{matrix} H\text{—}CH{=}N\text{—}OH \\ R\text{—}CH{=}NOH \end{matrix} \xrightarrow[\text{then heat}]{Cu^{+2},\ AcO^-} \begin{matrix} \phi\text{—}CHO \\ \phi\text{—}CO\text{—}R \end{matrix}$$

Yields of aldehydes or ketones are less than 50 per cent, but even this is sometimes higher than is obtained by other methods.

8. *Coupling reactions:*

The diazonium ion is a weak electrophilic reagent and reacts with aromatic rings containing very strong electron-releasing groups such as the OH, —O^-, NH_2, and NR_2 groups.



This reaction was mentioned in the chapter on phenols. Since the —O^- group is more electron-releasing than the OH group, phenols couple faster in alkaline solution than in acid. However, in alkaline solution, diazonium ions form diazohydroxides reversibly:

$$\phi\text{—}\overset{+}{N}\equiv N \underset{H_3O^+}{\overset{OH^-}{\rightleftharpoons}} \phi\text{—}N{=}N\text{—}OH$$

Benzene diazonium ion Benzenediazohydroxide

The diazohydroxides do not couple; hence the coupling reaction should not be done in a strongly alkaline reaction. Similarly, in coupling diazonium ions with amines, the solution should not be strongly acidic, in which all of the aniline is converted to anilinium ion, nor too basic to lose the diazonium ion. A compromise is reached such that coupling of diazonium salts is best done with amines in weakly acidic solutions and with phenols in mildly alkaline solutions.

Unsymmetrical azobenzenes can also be prepared by condensing nitrosobenzenes with aromatic primary amines:

$$\phi\text{—}N{=}O + \phi'\text{—}NH_2 \rightarrow \phi\text{—}N{=}N\text{—}\phi'$$

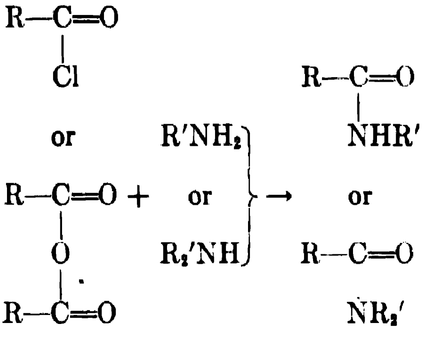
The preparation of nitrosobenzenes by the reduction of nitrobenzenes is taken up in Section 16.4b.

Secondary aromatic amines react with nitrous acid to yield blue N-nitroso compounds:

$$\phi_2NH + HONO \rightarrow \phi_2N\text{—}NO + H_2O$$

N-Nitroso-diphenyl amine

Acylation of amines: The reaction of amines with acid halides and anhydrides to give amides was discussed in Section 14.3.



$$\begin{array}{ccccc} R\text{—}C{=}O & & & & \\ | & & & & \\ Cl & & & & R\text{—}C{=}O \\ & & & & | \\ \text{or} & & R'NH_2 & & NHR' \\ R\text{—}C{=}O & + & \text{or} & \rightarrow & \text{or} \\ | & & & & \\ O & & R_2'NH & & R\text{—}C{=}O \\ | & & & & | \\ R\text{—}C{=}O & & & & NR_2' \end{array}$$

$$\phi\text{—}NH_2 + Ac_2O \rightarrow \phi\text{—}NHAc + AcOH$$

Acetanilide

Amides of a sulfonic acid are formed when an arylsulfonyl chloride is used:

$$\phi\text{—}SO_2Cl + H\text{—}NR_2 \rightarrow \phi SO_2NR_2 + HCl$$

This reaction forms the basis of distinguishing, as well as separating, primary, secondary and tertiary amines. Since the reaction consists of a replacement of a hydrogen atom on the nitrogen by a sulfonyl group, only the primary and secondary amines react:

$$\phi\text{—}SO_2Cl + H\text{—}NHR \longrightarrow \phi\text{—}SO_2NHR + HCl$$

Alkali soluble,
acid insoluble

$$\phi\text{—}SO_2Cl + H\text{—}NR_2 \longrightarrow \phi\text{—}SO_2NR_2 + HCl$$

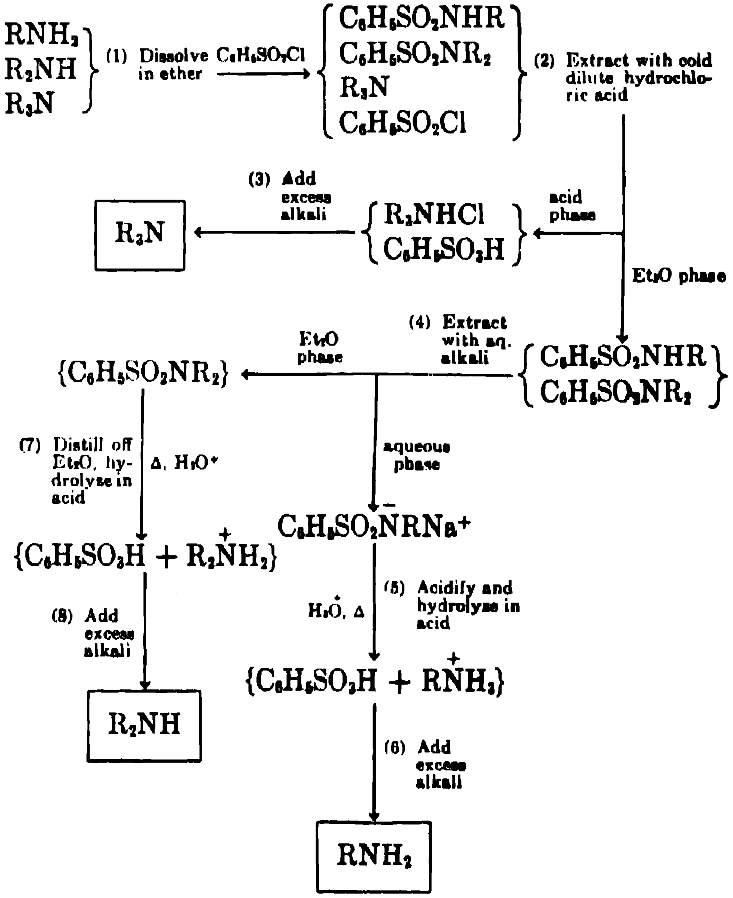
Alkali and acid
insoluble

$$\phi\text{—}SO_2Cl + NR_3 \not\longrightarrow \text{No reaction: } NR_3 \text{ remains}$$

Acid soluble,
alkali insoluble

Thus, if the product is insoluble in dilute alkali but soluble in dilute acid, it is the unreacted tertiary amine; if the product is insoluble in acid and base, it is the amide of a secondary amine; and if the product is insoluble in acid but soluble in alkali, it is the amide of a primary amine. These three solubility characteristics are different and distinguish the three classes of amines. These distinct differences in solubility may be used to resolve mixtures of the three classes of amines, called the *Hinsberg* separation.

Hinsberg separation of amines:



Any quaternary ammonium salt in the mixture is immediately removed when the mixture is dissolved in ether; the salt is ether insoluble. The ether solution is then treated with benzenesulfonyl chloride, and only the primary and secondary amines react. When this solution is extracted with dilute hydrochloric acid, unreacted benzenesulfonyl chloride hydrolyzes to the water-soluble benzenesulfonic acid, and the tertiary amine forms a water-soluble hydrochloride salt. This aqueous phase is then made alkaline (step 3) to liberate the tertiary amine as the free base. Then the ether solution of the sulfonamides from the primary and secondary amines is extracted with alkali (step 4). The amide of the primary amine is acidic and goes into the aqueous alkaline phase.[6] This solution is acidified (step 5), refluxed to hydrolyze the amide, and made alkaline (step 6) to liberate the free base, RNH_2. The ether solution of the amide from the secondary amine is distilled (step 7) to remove the solvent, the residue is acidified and heated under reflux to hydrolyze the amide, then made alkaline (step 8) to liberate the secondary amine.

Another use of the acylation products of amines is the conversion of the amines to the corresponding halides. In this case, benzoyl chloride, C_6H_5COCl is used.

$$RNH_2 \xrightarrow{C_6H_5COCl} RNH{-}COC_6H_5 \xrightarrow{PX_5} RX$$

The last step is known as the *von Braun reaction.*

Oxidation of amines: The oxidation of tertiary amines with aqueous hydrogen peroxide yields amine oxides.

$$R_3N + H_2O_2 \rightarrow R_3\overset{+}{N}{-}O^- + H_2O$$

The bond between nitrogen and oxygen is a coordinate covalent bond (also known as a *semicovalent* or *dative bond*) from which there are formal charges on the nitrogen and oxygen atoms as shown. This gives the amine oxides considerable saltlike character, as shown by their high boiling points, water solubilities, and ether insolubilities. For example, trimethylamine boils at 4° and is soluble in ether, in contrast to trimethylamine oxide which melts at 208° and is insoluble in ether. The basic character of the oxygen is revealed by its nucleophilic displacement reactions with alkyl halides and its salt formation with acids.

$$R_3\overset{+}{N}{-}O^- + R'X \rightarrow (R_3\overset{+}{N}{-}OR')X^- \qquad \text{Trialkyl-alkoxyammonium halide}$$

$$R_3\overset{+}{N}{-}O^- + HX \rightarrow (R_3\overset{+}{N}{-}OH)X^- \qquad \text{Trialkyl-hydroxylammonium halide}$$

The reactions of the first product with sodium hydroxide and of the second product with sodium alkoxide yield two isomeric compounds.

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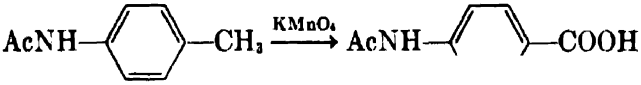
[6] Benzenesulfonamides of aliphatic and alicyclic primary amines with more than six carbon atoms are usually insoluble in aq. alkali. P. E. Fanta and C. S. Wang, *J. Chem. Educ.*, 41, 280 (1964).

$$(R_3\overset{+}{N}{-}OR')X^- \xrightarrow{NaOH} (R_3\overset{+}{N}{-}OR')OH^-$$

$$(R_3\overset{+}{N}{-}OH)X^- \xrightarrow{NaOR'} (R_3\overset{+}{N}{-}OH)\overset{-}{O}R'$$

This demonstrates that four of the bonds to nitrogen are of one type (covalent), and that the fifth is different (ionic).

Aromatic amines are easily oxidized, and most oxidizing agents convert the amines into quinones and other oxidation products. Sodium perborate in glacial acetic acid will oxidize substituted anilines to the corresponding azobenzenes in low yields. Acylation stabilizes the amine, and sufficiently so to permit the oxidation of a CH_3 group without oxidizing the rest of the molecule.



Reaction of chloroform with primary amines: When heated with chloroform in alkaline media, primary amines produce isocyanides.

$$RNH_2 + CHCl_3 + 3NaOH \rightarrow \underset{\text{An isocyanide}}{R{-}NC} + 3H_2O + 3NaCl$$

The isocyanides are readily detectable by their strong, garlic-like odors.

Active hydrogen atoms: Primary and secondary amines react with such reagents as Grignards, sodium metal, and acid halides and anhydrides in the same fashion as does water. Except for sodium metal, equations for these reactions have been given several times in connection with these reagents.

$$RNH_2 + Na \rightarrow RNHNa + \tfrac{1}{2}H_2$$

Lacking nitrogen-attached hydrogen atoms, tertiary amines cannot react in this way, but they do react as bases. Thus, they coordinate with metal ions, including Grignards, and may even serve as solvents for Grignards in place of ethers.

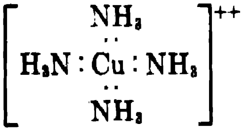
Complexation: Aliphatic amines form complexes with metal cations just as does ammonia:

$$\left[H_3N : Ag : NH_3\right]^+$$

Silver-ammonia complex

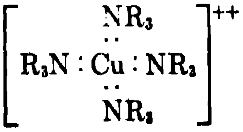
$$\left[R_3N : Ag : NR_3\right]^+$$

Silver-amine complex



$$\left[\begin{array}{c} NH_3 \\ \cdot\cdot \\ H_3N : Cu : NH_3 \\ \cdot\cdot \\ NH_3 \end{array}\right]^{++}$$

Copper-ammonia complex



$$\left[\begin{array}{c} NR_3 \\ \cdot\cdot \\ R_3N : Cu : NR_3 \\ \cdot\cdot \\ NR_3 \end{array}\right]^{++}$$

Copper-amine complex

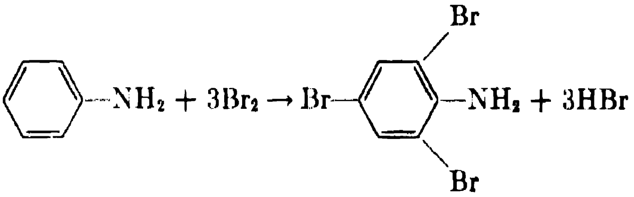
$Cu^{++} + 4NH_3 \rightleftarrows Cu(NH_3)_4^{++}$ $\quad$ $Cu^{++} + 4R_3N \rightleftarrows Cu(R_3N)_4^{++}$

$Ag^+ + 2NH_3 \rightleftarrows Ag(NH_3)_2^+$ $\quad$ $Ag^+ + 2R_3N \rightleftarrows Ag(R_3N)_2^+$

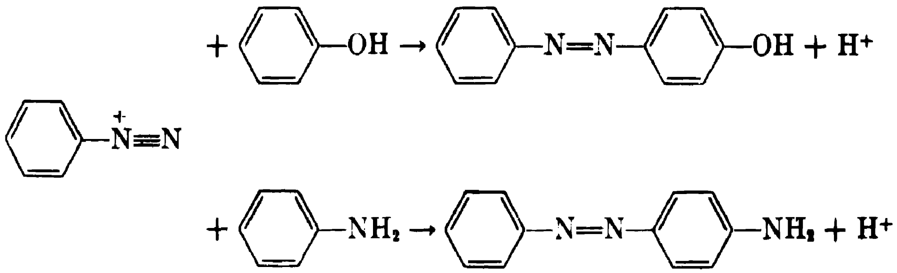
Hence, concentrated solutions of amines prevent the precipitation of copper hydroxide and silver oxide from alkaline solutions. In all these comparisons with ammonia, R_3N is used to represent primary, secondary, and tertiary amines, since all three classes behave similarly with respect to complex formation in the absence of steric effects.

On the other hand, amines differ from ammonia in the fact that ammonia does not burn in air, and amines do. The first few amines have odors resembling that of ammonia, and upon going up the homologous series the odors change to a fishlike odor, and finally to very repugnant odors. Amines form charge-transfer complexes (page 469) with polynitro compounds and often the picrates are used as derivatives.

Aromatic amines undergo some additional reactions because of the presence of the aromatic ring. The amino group is very strongly ring-activating; and aniline, like phenol, yields a tribromo product very rapidly:



Diazonium salts couple with phenols and anilines to give azo compounds:



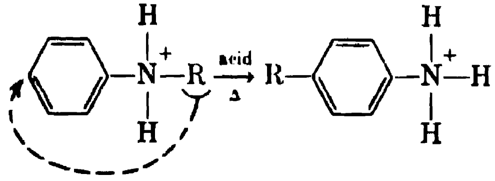
This reaction takes place with only a trace of phenol or aniline and provides a qualitative test for primary aromatic amines. An unknown is treated with cold nitrous acid and then added to an alkaline solution of a phenol. If the unknown is an aromatic primary amine, it will be diazotized by the nitrous acid, and in the alkaline solution, the diazonium ion will couple with the phenol to give a bright red color. If the unknown is not an aromatic primary amine, a diazonium ion would not be formed, nor would a deep coloration appear. This reaction provides a second method of making unsymmetrical azobenzenes. (See page 411.)

$$\phi\text{—}N_2^+ + \phi'\text{—}NH_2 \xrightarrow{\text{base}} \phi\text{—}N{=}N\text{—}\phi'\text{—}NH_2$$

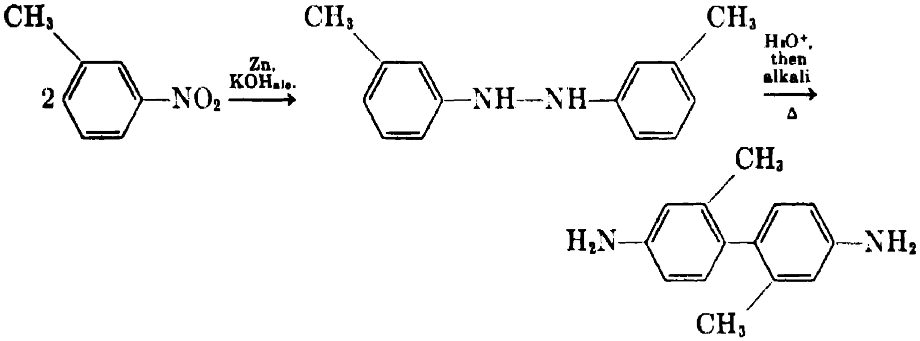
The amino group may be removed by deamination, if it is so desired. Symmetrical azobenzenes are prepared by reduction of nitrobenzenes with $LiAlH_4$ (cf. Table 16.4).

Hofmann rearrangement

When heated in strong acid media, N-substituted anilines suffer a rearrangement, and the substituent migrates to the *para* position. If the *para* position is already occupied, a small amount of *ortho* rearrangement will take place.

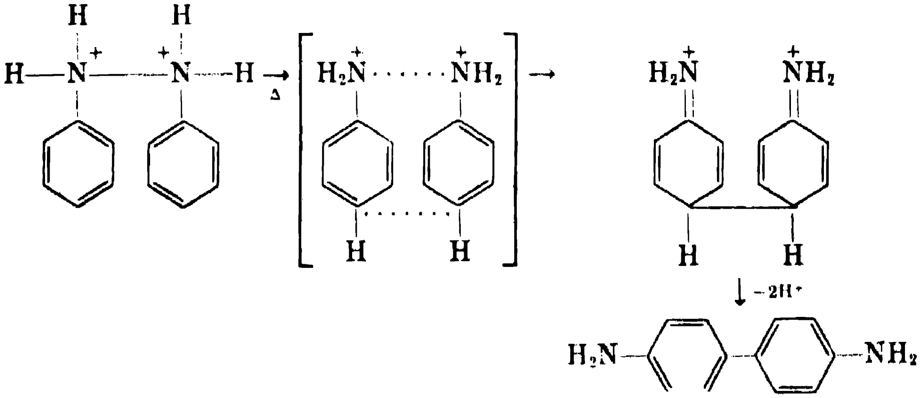


This reaction may be used for the preparation of symmetrical biphenyls from nitrobenzenes. Reduction of a nitrobenzene with Zn—$KOH_{alc.}$ yields the respective hydrazobenzene, which may then be subjected to a Hofmann rearrangement to yield a *p,p'*-diaminobiphenyl.

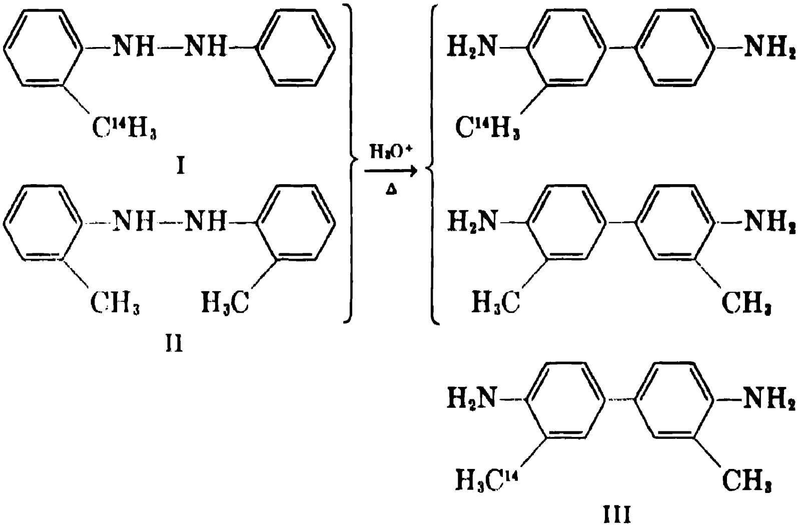


Since the products are substituted benzidines, the reaction is known as the *benzidine rearrangement.* If it is desired, the amino groups may be removed by deamination.

The benzidine rearrangement is an *intramolecular* reaction involving the diammonium salt.

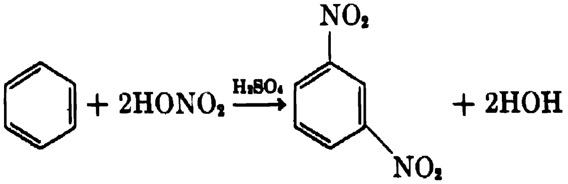


Several techniques have shown that the reaction is intramolecular and not intermolecular. The point is to show that the hydrazobenzene does not split into two fragments and then fragments from different molecules combine. The strongest evidence comes from experiments in which a mixture of two different hydrazobenzenes is used. For example, with I and II, in which I is labeled with C^{14}, less than 0.03 per cent of the crossover product III is obtained.



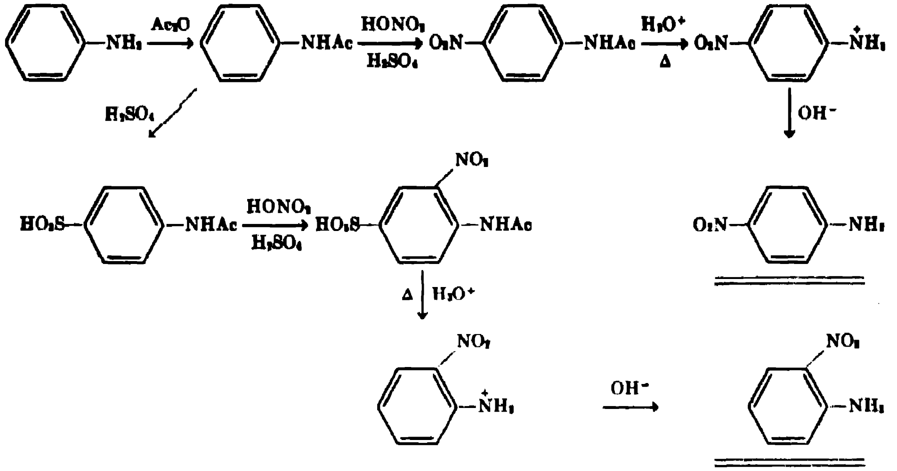
e. Uses of amines. Amines are used commercially for producing amides to be used as detergents. Amine salts of carboxylic acids are used extensively as herbicides. Aryl amines are used extensively as intermediates for the commercial production of dyes, drugs, photographic developers, and textiles. They are also used as antioxidants in rubber. They serve, too, as starting materials for the synthesis of many compounds by way of the diazotization reaction. In fact, the nitroanilines are such strategic compounds for the preparation of other classes of compounds that the student should be certain that he can prepare them from benzene. For the student's benefit, the preparation of the nitroanilines will be discussed here.

m-Nitroaniline. The easiest to prepare of the three isomers is *m*-nitroaniline, because *m*-dinitrobenzene is produced directly by the nitration of benzene.



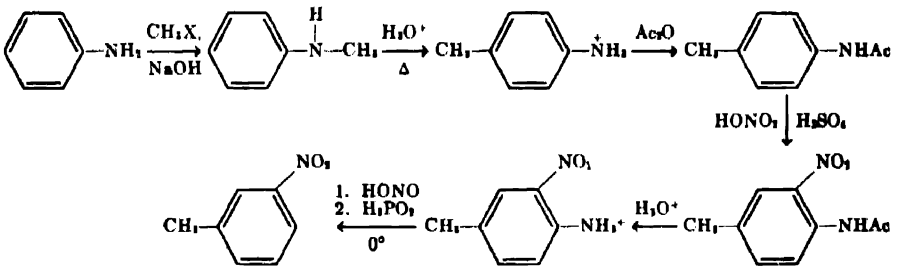
m-Nitroaniline is prepared from dinitrobenzene with enough reducing agent to reduce only one nitro group. Also, since aniline forms the salt in acid solution and the NH_3^+ group is *m*-orienting, aniline gives *m*-nitroaniline upon nitration in concentrated sulfuric acid. The yield is low, however, owing to oxidation of the aniline salt.

o- and p-Nitroanilines.



Aniline is first acetylated, and then either nitrated or sulfonated. The —NHAc group is *o,p*-directing, but the *para* isomer predominates. The acetyl group may be hydrolyzed off readily upon heating in acid or alkali. For making the *o*-nitroaniline, the *para* position is blocked with the —SO_3H group, which is later removed upon heating in mineral acid.

It is difficult to make *m*-nitrotoluene, and a demonstration of its preparation will be beneficial to the student.



Aniline is prepared from benzene by nitration and reduction of the nitro group. Aniline is then alkylated, the N-methylaniline carried through a Hofmann rearrangement, and the resulting methylaniline acetylated. Although two products may result from its nitration, the NHAc group has the stronger directing influence, so *p*-CH_3—C_6H_4—NHAc yields mostly 2-nitro-4-methylacetanilide. This is then hydrolyzed and deaminated.

It is to be noted that the reduction of nitro groups and the oxidation of alkyl groups take place by one group at a time. Thus, when there are two nitro groups on the ring, one may be reduced without affecting the other by using just enough reducing agent for one group. Similarly, one alkyl group is oxidized to a carboxyl group before a second group suffers oxidation. This should be done only when the alkyl groups are the same, because the preferential oxidation of alkyl groups is not always possible.[6]

The student is now capable of developing many syntheses. To forewarn him, the following precautions are given:

1. Do not diazotize ϕ—NO_2 for ϕ—NH_2.
2. Do not nitrate with HONO for $HONO_2$.
3. Do not carry out reactions with diazonium ions other than replacements of the diazonium group; that is, do not attempt to nitrate or brominate a diazonium salt.
4. When diazotizing a diamino compound, plan to diazotize both amino groups (tetrazotization); otherwise the second amino group would cause the diazonium salt to condense with itself.
5. When possible, prepare alkyl benzenes by the Friedel-Crafts reaction rather than through the use of the two successive steps, halogenation and Wurtz-Fittig reaction.

STUDY EXERCISES

1. Illustrate by general equations (a) the alkylation of ammonia, (b) Gabriel's synthesis of amines, (c) the Hofmann reaction.

2. Illustrate by general equations the reactions of nitrous acid with (a) primary and secondary amines, (b) primary and secondary nitroalkanes, (c) *n*-butyramide.

3. Describe how nitrous acid could be used to distinguish primary, secondary, and tertiary amines.

4. Write general equations for (a) the acid reduction of nitrotoluene to toluidine; (b) diazotization of aniline; (c) acetylation of aniline; (d) replacement of the diazonium group by OH, H, I, Br, F, NO_2, and ϕ; (e) a Hofmann rearrangement; (f) coupling of a diazonium salt with aniline; (g) the preparation of *o*-, *m*-, and *p*-nitroanilines.

5. Illustrate by equations the reactions between aniline and (a) ethyl iodide, (b) propionyl chloride, (c) acetic anhydride, (d) cold nitrous acid.

6. Is an aqueous solution of diethylamine hydrochloride acidic or basic? Why?

7. Describe the Hinsberg method of separating primary, secondary, and tertiary amines.

8. Which has the smaller concentration of cupric ions, a solution of copper nitrate to which an excess of sodium hydroxide has been added or a solution of copper nitrate to which an excess of ammonia has been added? On what basis do you give your answer?

9. How can the following substances be distinguished from each other by qualitative test-tube experiments: (a) $C_3H_7NH_2$, (b) $C_2H_5NHCH_3$, (c) $(CH_3)_3N$?

10. Predict which isomeric amine has the greater solubility in water and give the basis of your answer, trimethylamine or methylethylamine.

11. Explain through the use of structural formulas why benzenediazonium ions undergo nucleophilic substitution reactions:

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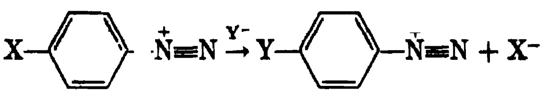
[6] However, see L. N. Ferguson and A. I. Wims, *J. Org. Chem.*, **25**, 668 (1960).



TEST QUESTIONS, Set 16

1. What is the *p*H of a 0.1 *N* aqueous solution of diethylamine? $K_b = 1.26 \times 10^{-3}$.

2. Indicate the sequence of reactions one could use in the laboratory to convert propyl iodide into propylamine, and what weight of propylamine could be produced from 17 g of propyl iodide if each step takes place in a 90% yield?

3. Work problem 2 for the conversion of propyl iodide into *n*-butylamine.

4. What volume of nitrogen gas, measured at 745 mm and 25°, will be collected if 0.15 g of butylamine is treated with nitrous acid, and the nitrogen is collected with 98% efficiency?

5. What is the molecular weight of a monoamine if a 0.22-g sample produces 59.9 ml of N_2, measured at 25° and 738 mm, assuming the per cent efficiency of collection of nitrogen is 95%?

6. A 10-g sample of urine was treated with nitrous acid and the N_2 collected over concentrated KOH. When the volume of the gas was corrected to standard conditions, it was found to occupy a volume of 89.6 ml. What was the percentage of urea, $(H_2N)_2CO$, in the sample?

7. What is the concentration of hydroxide ion in 200 ml of an aqueous solution containing 5 g of isoamylamine? $K_b = 5 \times 10^{-4}$.

8. How could one separate and isolate the components in a mixture of octanoic acid, *n*-octylamine, and 2-octanol without resorting to fractional distillation other than the separation from ether or chloroform?

9. What series of laboratory reactions could be used to convert methyl *n*-propyl ketone to *n*-propylamine?

10. What are two different qualitative test-tube experiments which could be used to distinguish pure samples of the isomeric amines, *n*-pentylamine and ethyl-*n*-propylamine?

11. Indicate the series of reactions one could use in the laboratory to prepare each of the following, starting with benzene in each case: (a) *m*-chloroaniline; (b) *m*-fluorobenzoic acid; (c) 3,4′-dimethylbiphenyl; (d) 3-iodo-4′-methylazobenzene; (e) 4-chloro-4′-bromoazobenzene; (f) *m*-bromobiphenyl; (g) 2,6-dinitrophenol; (h) 3,3′-diiodoazobenzene; (i) *o*-dinitrobenzene; (j) 1,3,5-tribromobenzene.

12. How could one separate and isolate the components in the following mixtures without using fractional distillation other than the separation from ether: (a) salicylaldehyde, *p*-hydroxybenzaldehyde, N-methylaniline, benzaldehyde, and toluene; (b) *p*-chlorophenol, *p*-chloroaniline, *p*-chloro-N-methylaniline, and *p*-chloronitrobenzene?

13. How can the following be distinguished by qualitative test-tube experiments: (a) $C_6H_5NH_3Cl$ from Cl—C_6H_4—NH_2, (b) CH_3—C_6H_4—NH_2 from $C_6H_5NHCH_3$?

14. Starting with a substituted nitrobenzene, how could 3,3′-diethylbiphenyl be prepared in the laboratory?

15. If a water solution of benzenediazonium chloride shows the presence of chloride ion and is neutral, what is known regarding the strength of the base benzenediazonium hydroxide, $\phi N_2^+OH^-$?

16. What weight of iron is necessary to reduce 100 g of nitrotoluene to toluidine in acid solution?

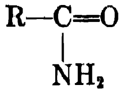
17. What is the relative order of basicity of aniline, *p*-nitroaniline, N-methylaniline, and cyclohexylamine?

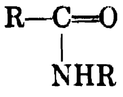
18. Offer an explanation for the observation that benzenediazonium chloride does

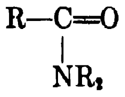
not couple with anisole but 2,4-dinitrobenzenediazonium chloride does. On this basis, should *p*-toluenediazonium ion couple as readily as benzenediazonium ion?

16.2 AMIDES

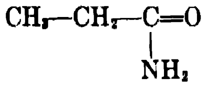
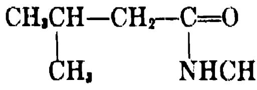
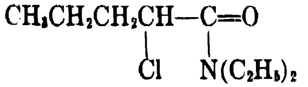
An amide is a compound having an acyl group attached to an amino nitrogen atom.

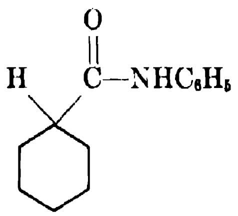

$R{-}C(=O){-}NH_2$

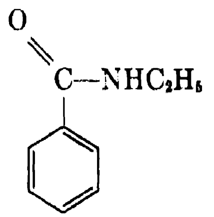

$R{-}C(=O){-}NHR$

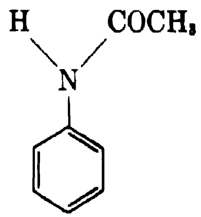

$R{-}C(=O){-}NR_2$

a. Nomenclature of amides. Amides are named under the Geneva system by changing the *-e* ending of the parent hydrocarbon to *-amide*. The common names of amides stem from the names of the corresponding acids with the *-ic* suffix replaced by *-amide*. When alkyl groups are attached to the nitrogen atom, they are so indicated by the capital N. The following examples will serve to illustrate these procedures.

Structure	*I.U.C. Name*	*Common Name*
 $CH_3{-}CH_2{-}C(=O){-}NH_2$	Propanamide	Propionamide
 $CH_3CH(CH_3){-}CH_2{-}C(=O){-}NHCH_3$	N-Methyl 3-methylbutanamide	N-Methyl β-methylbutyramide
 $CH_3CH_2CH_2CH(Cl){-}C(=O){-}N(C_2H_5)_2$	N,N-Diethyl 2-chloropentanamide	N,N-Diethyl α-chlorovaleramide

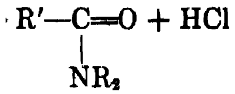

N-Phenylcyclohexane carboxamide


N-Ethyl benzamide

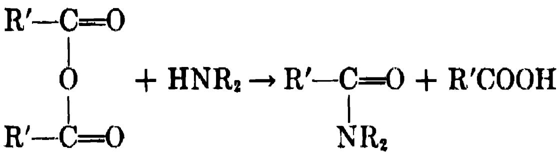

Acetanilide

b. Preparation of amides.

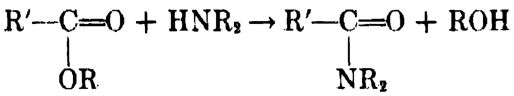
Acylation of ammonia or amines: Either esters, anhydrides, or acid halides may be used to acylate an amine. Acid halides react vigorously, anhydrides react readily, and esters react slowly. With an acid halide then, the reaction is usually moderated by the use of an inert solvent (a hydrocarbon, for this purpose).



$$R'-\underset{\substack{|\\ NR_2}}{C}=O + HCl$$

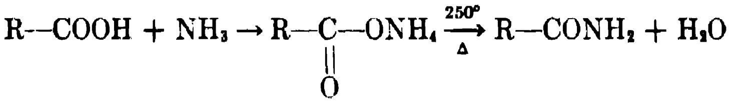


$$\begin{array}{c}R'-C=O\\ |\\ O\\ |\\ R'-C=O\end{array} + HNR_2 \rightarrow R'-\underset{\substack{|\\ NR_2}}{C}=O + R'COOH$$



$$R'-\underset{\substack{|\\ OR}}{C}=O + HNR_2 \rightarrow R'-\underset{\substack{|\\ NR_2}}{C}=O + ROH$$

In industry, ammonium salts are pyrolyzed to yield amides:



$$R-COOH + NH_3 \rightarrow R-\underset{\substack{\|\\ O}}{C}-ONH_4 \xrightarrow[\Delta]{250^\circ} R-CONH_2 + H_2O$$

but in the laboratory, it is more convenient to use one of the above acylating agents.

Hydrolysis of nitriles: Nitriles may be partially hydrolyzed under controlled conditions to yield amides. One procedure is to use an alkaline solution of hydrogen peroxide,

$$RCN + 2H_2O_2 \xrightarrow{OH^-} RCONH_2 + H_2O + O_2$$

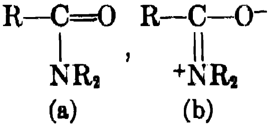
and another is to use polyphosphoric acid as the catalyst and solvent.

c. Physical and chemical properties of amides. Amides are neutral compounds; hence the attachment of the acyl group to nitrogen has markedly lowered the basicity of the nitrogen atom. Because of a large ionic character and intermolecular hydrogen bonding, most amides are solids (cf. Table 16.2).

TABLE 16.2. PHYSICAL CONSTANTS OF SOME AMIDES

Name	*Melting Point*	*Name*	*Melting Point*
Formamide	3	Acetanilide	114
Acetamide	82	Benzanilide	163
Propionamide	79	Aceto-*p*-toluidide	147
n-Butyramide	116	*p*-Nitroacetanilide	216
n-Valeramide	106	Sulfanilamide	163

Amides are resonance hybrids of structures (a) and (b) with a large contribution from (b).



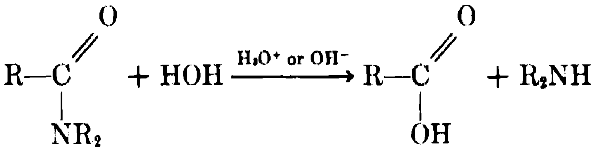
$$\underset{(a)}{R-\underset{\substack{|\\ NR_2}}{C}=O}, \quad \underset{(b)}{R-\underset{\substack{\|\\ {}^{+}NR_2}}{C}-O^-}$$

Evidence for the contribution of form (b) is provided by the fact that the carbon-nitrogen bond (1.38 Å) is shorter than a normal C—N bond (1.47 Å) and the carbon-oxygen bond (1.28 Å) is longer than a typical carbonyl bond (1.21 Å). That is, the carbon-nitrogen bond is neither a real C—N single bond nor a C═N double bond, but something in between which cannot be drawn. In other words, the actual structure is neither (a) nor (b), but some intermediate structure not representable by a single structural formula. Dipole moments and other physical properties verify the large ionic character of amides.

Because of association with water through hydrogen bonding and to a large ionic character, the amides up to valeramide are soluble in water. Not until the hydrocarbon chain is three carbons in length are the amides soluble in ether. Formamide is one of the very few liquids having a larger dielectric constant than water, and accordingly, formamide is a good ionizing solvent. Dimethylformamide is even better as a general solvent, owing to its greater stability. For example, dimethylformamide dissolves salts and polar compounds like polyhydric alcohols (usually insoluble in ether) as well as fats (insoluble in water), and is a good solvent for conducting acetylations, chlorinations, sulfonations, polymerizations, and acid-base titrations.

The amides are sharp-melting crystalline compounds and make good derivatives for any of the acyl classes of compounds, i.e., esters, acids, acid halides, anhydrides, and lactones.

Hydrolysis of amides: Like the other acyl compounds, amides suffer hydrolysis upon refluxing in water. The reaction is catalyzed by acid or alkali.



$$R\text{—}C(=O)NR_2 + HOH \xrightarrow{H_3O^+ \text{ or } OH^-} R\text{—}C(=O)OH + R_2NH$$

The reaction is usually quantitative, and a titration of the acid or base liberated may be used for a determination of the equivalent weight of the amide, or for its quantitative analysis.

Dehydration of amides: Primary amides may be dehydrated to yield nitriles.

$$R\text{—}CONH_2 + C_6H_5SO_2Cl \xrightarrow[70^\circ]{\text{pyridine}} R\text{—}CN + C_6H_5SO_3H + HCl$$

The reaction is run in pyridine, which takes up the two acids in the form of their pyridine salts. Other dehydrating agents, such as P_2O_5, may be used but are not as convenient to handle.

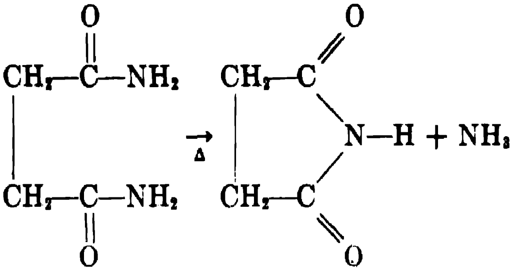
Reaction with nitrous acid: Primary and secondary amides of the type $RCONH_2$ and RCONHR react with nitrous acid in the same way as do the corresponding primary and secondary amines.

$$RCONH_2 + HONO \rightarrow RCOOH + N_2 + HOH$$

$$RCONHR + HONO \rightarrow RCON(NO)R + HOH$$

Conversion of amides to amines: The reduction of amides to amines with $LiAlH_4$, and Hofmann's degradation of amides to amines were discussed in Section 16.1b.

Conversion of amides to imides: When diamides with their amide groups close together are heated, they lose ammonia to yield imides.



Succinimide

Imides are compounds having two acyl groups attached to a single amino nitrogen atom. The most common imides are succinimide and phthalimide in which the two acyl groups are joined.

Imides are weak acids with K_a's about 10^{-10}. Hence they dissolve in concentrated alkali and the hydrogen atom can be replaced by a metal cation. An example is potassium phthalimide, which is used in the Gabriel synthesis (page 399). N-Bromoimides are useful as brominating agents, particularly for brominations that proceed by free radical mechanisms.

Like amides, imides hydrolyze in acid or alkali, but imides give two equivalents of acid and one equivalent of base per mole of imide.

d. Uses of amides. Amides are used in a wide variety of ways. Nylon is a polyamide; Sucaryl, the sweetening agent, is an amide (saccharin is an imide); the substituted ureas are powerful herbicidal agents, and some amides are used as detergents.

16.3 ALKYL CYANIDES AND ISOCYANIDES

a. Nomenclature. Alkyl cyanides are alkyl derivatives of hydrogen cyanide. They are named by giving the name of the alkyl group, and adding the word *cyanide*. For complex compounds, cyanides may be considered as cyano derivatives of other classes of compounds. Alkyl cyanides are also called *nitriles*, based on the name of the acid which would be formed upon hydrolysis. Several examples follow:

CH_3CN	Methyl cyanide or acetonitrile
$CH_2{=}CH{-}CN$	Vinyl cyanide or acrylonitrile
CH_3CH_2CN	Ethyl cyanide or propionitrile
$(CH_3)_2CHCN$	Isopropyl cyanide or isobutyronitrile

The isocyanides (isonitriles or carbylamines) are isomers of cyanides and are named as alkyl isocyanides or alkyl isonitriles. Thus, CH_3NC is methyl isocyanide or methyl isonitrile.

b. Preparation of cyanides and isocyanides.

From alkyl halides:

$$R{-}X + KCN \rightarrow R{-}CN + KX$$

$$R{-}X + AgCN \rightarrow R{-}NC + AgX$$

The cyanide ion, $:\overset{-}{C{\equiv}N}:$, has an unshared pair of electrons on both ends. With potassium cyanide, the major product is the alkyl cyanide; with silver cyanide, the chief product is the alkyl isocyanide. In both reactions, however, some of the other isomer is also produced.

Cyanides from amides and aldoximes: The dehydration of amides to nitriles was given in Section 16.2c when the properties of amides were discussed.

$$R{-}CONH_2 \xrightarrow{\text{D.A.}} RCN + H_2O \qquad \text{D.A.} = C_6H_5SO_2Cl,\ SOCl_2,\ \text{or}\ P_2O_5$$

Acetic anhydride is usually used to dehydrate aldoximes.

$$RCH{=}NOH + (CH_3CO)_2O \rightarrow R{-}CN + 2CH_3COOH$$

Isocyanides from amines: The reaction of primary amines with chloroform and alkali to yield isocyanides was given among the chemical properties of amines.

$$RNH_2 + CHCl_3 + NaOH \rightarrow R{-}NC + 3NaCl + 3H_2O$$

c. Properties of cyanides and isocyanides. Cyanides are fairly polar compounds, as shown by the data in Table 10.7, but they are less soluble in water than amines. For example, nitriles higher than propionitrile are only slightly soluble in water. They are much weaker bases than amines, too, for they are not soluble in aqueous acids.

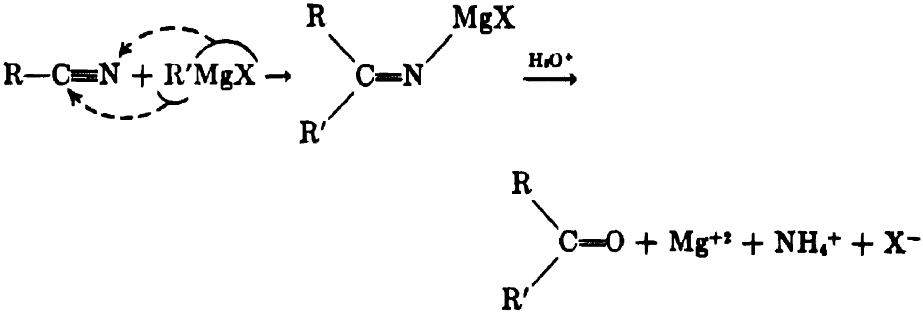
Alkyl cyanides have pleasant odors and are only slightly toxic, in direct contrast to isocyanides, which have very disagreeable odors and are highly toxic. Isocyanides boil at lower temperatures than their isomeric cyanides.

Hydrolysis: Cyanides hydrolyze to carboxylic acids and ammonia, whereas isocyanides yield amines and formic acid.

$$R-CN + 2H_2O \xrightarrow{H_3O^+ \text{ or } OH^-} RCOOH + NH_3$$

$$R-NC + 2H_2O \xrightarrow{H_3O^+ \text{ or } OH^-} RNH_2 + HCOOH$$

Addition of Grignards: Nitriles add Grignard reagents, and the products may be hydrolyzed to yield ketones.



Reduction: The reduction of nitriles to primary amines was first given in Section 16.1b.

$$R-CN \xrightarrow{R.A.} RCH_2NH_2$$

R.A. = $LiAlH_4$
Na, alcohol
H_2, cat.

$$R-NC \xrightarrow{R.A.} RNHCH_3$$

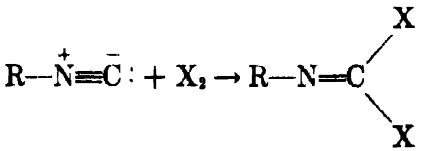
R.A. = NaHg
H_2, cat.

The fact that isocyanides yield secondary amines provides evidence that the nitrogen atom in alkyl isocyanides is attached to the alkyl group.

Oxidation of isocyanides: Mild oxidizing agents convert isocyanides to isocyanates.

$$R-\overset{+}{N}\equiv C^- + HgO \rightarrow \underset{\text{Alkyl isocyanate}}{R-N=C=O} + Hg$$

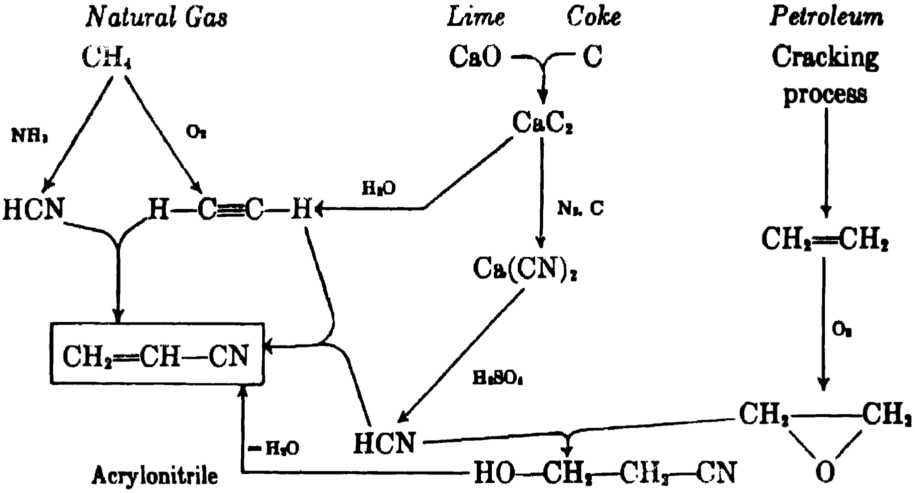
The fact that halogens add to isocyanides was formerly given as evidence of a divalent carbon, R—N═C,



$$R-\overset{+}{N}\equiv\overset{-}{C}: + X_2 \rightarrow R-N=CX_2$$

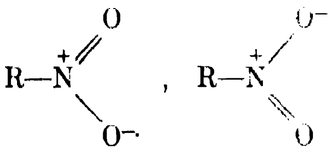
but now the electronic structure $R-\overset{+}{N}\equiv\overset{-}{C}:$ is believed to be the more important, based on the direction and magnitude of dipole moments of isocyanides. Thus, carbon is quadrivalent but one of the valences is ionic.

d. Uses of cyanides and isocyanides. With the exception of hydrogen cyanide and vinyl cyanide, the cyanides and isocyanides have no large-scale commercial uses yet. However, the cyanides are important intermediates in multistep syntheses in the laboratory. Millions of pounds of acrylonitrile (vinyl cyanide) are produced annually, principally for the production of nitrile rubbers (Section 3.6) and synthetic textiles (Chapter 26). Commercially, acrylonitrile is made from natural gas, coke and lime, or petroleum.



16.4 NITRO COMPOUNDS

a. Nitroalkanes. Nitroalkanes have the general formula R—NO_2 and are named by adding the prefix *nitro* to the name of the alkyl group, or as nitro derivatives of alkanes. The nitro group, attached directly to carbon, is a resonance hybrid of two equivalent structures.



This view is supported by the fact that the nitrogen-oxygen bond distances are identical, 1.21 Å, close to the normal N=O distance (1.18 Å), but much less than the normal N—O distance (1.36 Å).

1. Preparation. Commercially, nitroalkanes are prepared by the vapor-phase nitration of alkanes, already discussed on page 66, or by the liquid-phase nitration of olefins. Many nitration products are produced and are separated by distillation. In the laboratory, primary and secondary nitroalkanes are produced from the respective alkyl iodides or bromides:

$$R{-}Br + KNO_2 \rightarrow R{-}NO_2 + KBr$$

Most textbooks suggest the use of $AgNO_2$, but it has been shown[7] that KNO_2 or $NaNO_2$ are better, provided a solvent is used in which both the alkyl halide and nitrite salt are soluble.[8] Dimethylformamide and dimethylsulfoxide, $(CH_3)_2SO$, were found to be suitable solvents for this reaction. In any case, the major side product is the isomeric nitrite ester. Separation of the isomerides is easy because of the much higher boiling points of the nitroparaffins. See Table 16.3.

TABLE 16.3.

Nitroparaffin	B.P.	B.P.	Alkyl Nitrite
Nitromethane	101°	−12°	Methyl nitrite
Nitroethane	114	+17	Ethyl nitrite
1-Nitropropane	132	57	*n*-Propyl nitrite

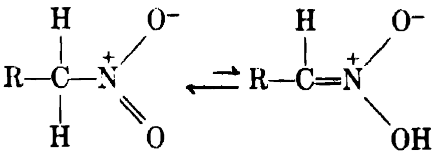
Tertiary nitroalkanes may be prepared by permanganate oxidation of the corresponding *t*-carbinamines.

$$R_3C—NH_2 \xrightarrow{MnO_4^-} R_3C—NO_2$$

2. ***Physical properties.*** The mononitroalkanes are colorless when pure. Because of the formal charges in the nitro group, the nitroalkanes are highly polar compounds, as shown by their large dipole moments (3.2D) and fairly high boiling points. Nitromethane is about 10 per cent soluble in water, but the higher nitroalkanes are practically insoluble. They make good solvents for other organic substances.

3. *Chemical properties.*

Salt formation: Nitroalkanes exhibit tautomerism in a manner analogous to ketones.



Nitro form *Aci* form

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[7] N. Kornblum *et al.*, *J. Org. Chem.*, **22**, 455 (1957). When it is expedient to do so, primary and secondary nitroalkanes may be produced by the oxidation of oximes with peroxytrifluoroacetic acid (W. D. Emmons and A. S. Pagano, *J. Am. Chem. Soc.*, **77**, 4557 (1955)).

$$R_2C{=}NOH \xrightarrow{CF_3CO_3H} R_2C{=}NO_2H \rightarrow R_2CHNO_2$$

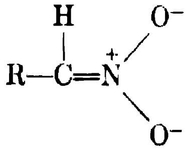
[8] The same situation occurs for the preparation of alkyl azides, RN_3, from alkyl halides and sodium azide. The yield is considerably improved if a solvent is used which dissolves both reactants (cf. E. Lieber *et al.*, *J. Org. Chem.*, **22**, 238 (1957)).

The *aci* form is a weak acid and will form salts with strong bases.

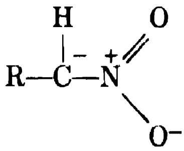
$$RCH_2NO_2 + NaOH \rightarrow RCHNO_2^-Na^+ + HOH$$

Secondary nitroalkanes, R_2CHNO_2, can also tautomerize to an *aci* form, but tertiary nitroalkanes, $R_3C—NO_2$, cannot, and therefore the latter compounds do not form salts. The primary and secondary nitroalkanes are called *pseudo acids* (false acids) because of the slowness with which they react with bases, whereas true acids react instantaneously with bases. On the other hand, the *aci* forms of nitroalkanes are true acids, for they react rapidly with bases. The rates of neutralization of nitroalkanes, then, depend on their rates of tautomerization to the *aci* forms. Aqueous solutions of *aci* tautomers are conducting, but the conductivity of aqueous solutions of nitro tautomers is negligible.

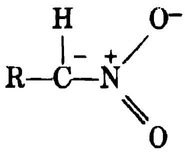
Tautomerism is not to be confused with resonance. Resonance does not involve a change in the positions of the atoms, only of the electrons. Tautomers may be isolated sometimes, but the forms contributing to resonance are imaginary and cannot be isolated. The anion of the *aci* form is a resonance hybrid of three forms.



(a)



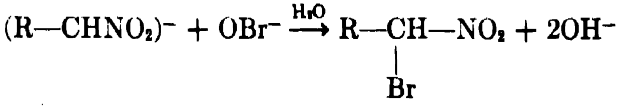
(b)



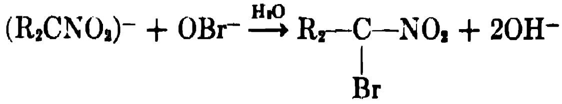
(c)

Form (a) makes the major contribution, and when acid is added it adds to an oxygen atom, giving the *aci* form. Under careful conditions the *aci* tautomer may be isolated, but slowly it tautomerizes back to the more stable *nitro* tautomer.

Bromination: Primary and secondary nitroalkanes, like aldehydes and ketones (page 325), brominate readily in alkaline solution:



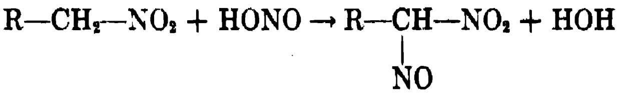
$$(R—CHNO_2)^- + OBr^- \xrightarrow{H_2O} R—\underset{\displaystyle Br}{\underset{|}{CH}}—NO_2 + 2OH^-$$



$$(R_2CNO_2)^- + OBr^- \xrightarrow{H_2O} R_2—\underset{\displaystyle Br}{\underset{|}{C}}—NO_2 + 2OH^-$$

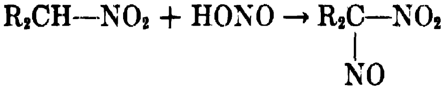
Only alpha halogenation takes place; hence, tertiary nitroalkanes are unreactive.

Reaction with nitrous acid: Primary and secondary nitroalkanes react with nitrous acid to give blue nitroso derivatives:



$$R\text{—}CH_2\text{—}NO_2 + HONO \rightarrow R\text{—}\underset{\overset{|}{NO}}{CH}\text{—}NO_2 + HOH$$

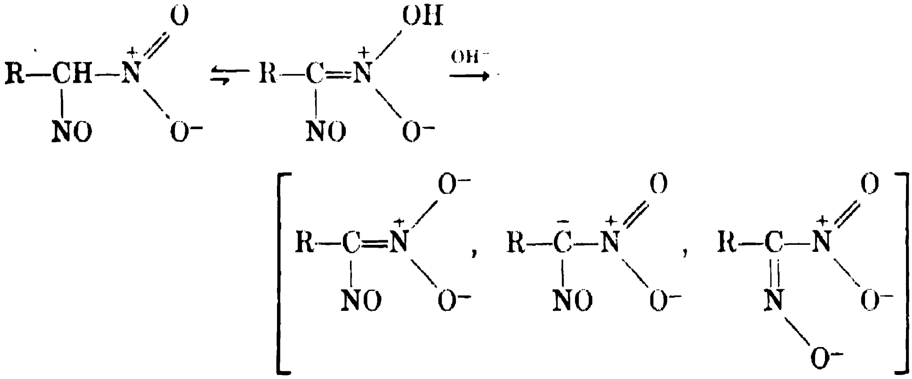
A nitrolic acid



$$R_2CH\text{—}NO_2 + HONO \rightarrow R_2\underset{\overset{|}{NO}}{C}\text{—}NO_2$$

$$R_3C\text{—}NO_2 + HONO \rightarrow \text{No reaction}$$

The nitroso derivative of the primary nitro compound, called a *nitrolic acid,* is soluble in alkali to give a red anion:



A resonance hybrid

The secondary nitroso nitro compound has no acidic hydrogen atom and is therefore insoluble in alkali as well as in water. The primary nitroalkane gives a blue product yielding a red alkaline solution, the secondary nitroalkane gives a blue, alkali-insoluble nitroso product, the tertiary nitroalkane does not react and remains colorless. This reaction with nitrous acid, therefore, offers a method of distinguishing the three classes of nitroalkanes. It is sometimes referred to as the *red, white,* and *blue reaction.*

Reduction of nitroalkanes: The reduction of nitroalkanes to amines was given in Section 16.1b as a method of preparing primary amines. Again, $LiAlH_4$, or zinc or tin in hydrochloric acid may be used.

Hydrolysis: The acid-catalyzed hydrolysis of primary nitroalkanes yields carboxylic acids and salts of hydroxylamine.

$$RCH_2NO_2 + HCl + HOH \rightarrow RCOOH + HONH_2 \cdot HCl$$

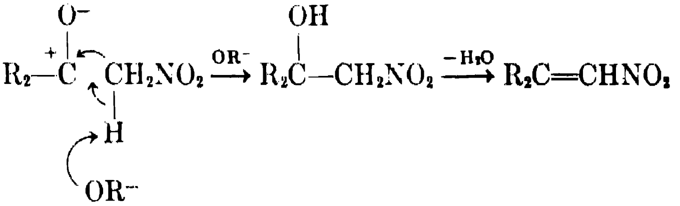
The reaction involves an oxidation of the carbon and a reduction of the nitro group. It is used for the commercial production of hydroxylamine, and for years it has been almost the sole method of producing hydroxylamine. More recently, Du Pont developed a method to produce hydroxylamine in a pure form from nitric oxide and hydrogen at low cost.

If the salt of the *aci* form of a primary or secondary nitroalkane is hydrolyzed in sulfuric acid, an aldehyde or ketone, and nitrous oxide are produced. This is called the *Nef reaction:*

$$R{-}CH{=}NO_2Na + H_2SO_4 \xrightarrow{0^\circ} R{-}CHO + \tfrac{1}{2}N_2O + NaHSO_4 + HOH$$

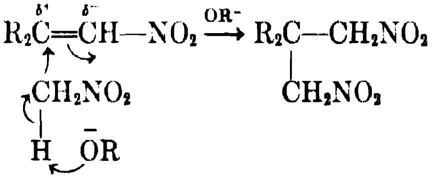
$$R_2C{=}NO_2Na + H_2SO_4 \xrightarrow{0^\circ} R_2C{=}O + \tfrac{1}{2}N_2O + NaHSO_4 + H_2O$$

Condensation with aldehydes and ketones: In the presence of bases, primary and secondary nitroalkanes condense with aldehydes and ketones. Under certain conditions, the nitroalcohols may be isolated, but usually a nitroolefin is obtained:



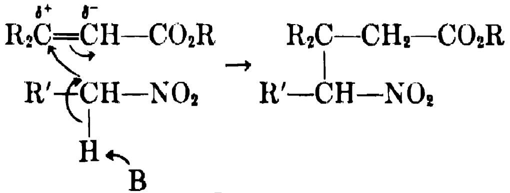
$$R_2\overset{O^-}{\underset{+}{C}}\;CH_2NO_2 \xrightarrow{OR^-} R_2\overset{OH}{C}{-}CH_2NO_2 \xrightarrow{-H_2O} R_2C{=}CHNO_2$$

This reaction is analogous to the aldol condensation of aldehydes and ketones. Then, often a second mole of nitroalkane will add to the nitroolefin.

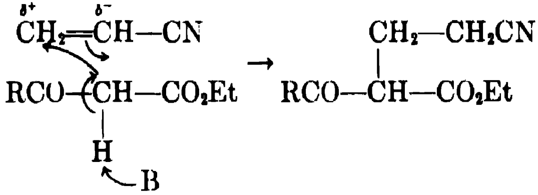


$$R_2\overset{\delta+}{C}{=}\overset{\delta-}{C}H{-}NO_2 \xrightarrow{OR^-} R_2\underset{CH_2NO_2}{C}{-}CH_2NO_2$$

This last step is really a *Michael condensation.* The base-catalyzed addition of activated C—H groups to α,β-unsaturated nitro, carbonyl, or cyanide compounds is referred to as the *Michael reaction.*

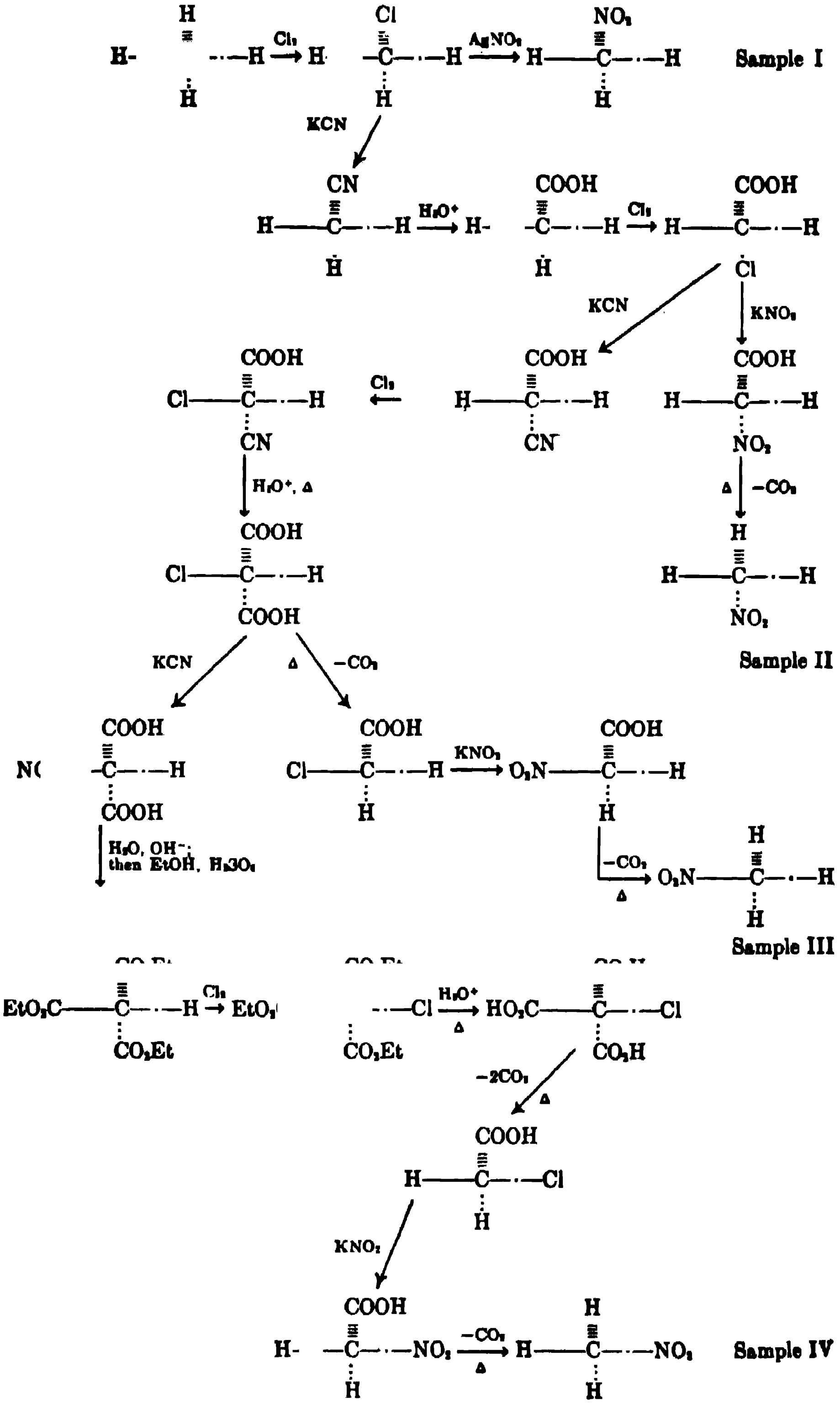


$$R_2\overset{\delta+}{C}{=}\overset{\delta-}{C}H{-}CO_2R \;\rightarrow\; R_2C{-}CH_2{-}CO_2R \;(R'{-}CH{-}NO_2)$$



$$\overset{\delta+}{C}H_2{=}\overset{\delta-}{C}H{-}CN \;\rightarrow\; CH_2{-}CH_2CN \;(RCO{-}CH{-}CO_2Et)$$

*4. **Uses of nitroalkanes.*** The principal industrial uses of nitroalkanes, other than for the production of hydroxylamine, have been as solvents in the plastics industry and as intermediates in the production of insecticides,


Cl₂
AgNO₃
Sample I
KCN
H₃O⁺
Cl₂
KCN
KNO₂
Cl₂
H₃O⁺, Δ
Δ
−CO₂
Sample II
KCN
Δ
−CO₂
KNO₂
H₂O, OH⁻; then EtOH, H₂SO₄
−CO₂
Δ
Sample III
Cl₂
H₃O⁺
Δ
−2CO₂
Δ
KNO₂
−CO₂
Δ
Sample IV

emulsifying agents, detergents, propellants, explosives, pharmaceuticals, and finish-removers. Many nitro compounds are violent explosives, particularly polynitro substances and nitroamines, and should not be handled except by directions from experienced chemists.

Chloropicrin, Cl_3CNO_2, is a powerful lachrymator and lung irritant and has been used in tear bombs. Tetranitromethane is sometimes used for the detection of carbon-carbon unsaturation. In dilute chloroform solutions, simple alkenes and alkynes give yellow colors, and the color deepens from orange to red with the increased unsaturation of conjugated polyenes.

Frequent mention has been made of the equivalency of the four bonds in CH_4. This is usually based on the failure to obtain isomers of monosubstituted methanes, such as isomers of CH_3Br, CH_3COOH, CH_3NH_2, etc., and on the success of a tetrahedral model of the carbon atom to account for the numbers of isomers obtained for various formulas. However, the British chemist, Louis Henry,[9] was able to show by an ingenious method that the four carbon bonds in CH_4 are equivalent. He synthesized four samples of nitromethane in which the nitro group had definitely replaced different hydrogen atoms. All four samples were nevertheless identical. Henry's method is diagramed on page 432. In the four samples of nitromethanes, I–IV, the nitro group is joined to carbon at different points, indicated by different lines of attachment. Still, each sample was found to be identical, proving that the four bonds to carbon are equivalent.

b. Nitrobenzenes.

1. Preparation.

Direct nitration:

$$\phi\text{—H} + HONO_2 \xrightarrow{H_2SO_4} \phi\text{—NO}_2 + HOH$$

Nitration is usually carried out with concentrated nitric and sulfuric acids in a 1:1 volume ratio. The higher the temperature and the stronger the nitric acid, the greater is the chance for polynitration. Other nitrating agents, such as acetyl nitrate or $KNO_3 + H_2SO_4$ may be used.

Replacement of the diazonium group:

$$\phi\text{—N}_2BF_4 + NO_2^- \xrightarrow{Cu} \phi\text{—NO}_2 + N_2 + BF_4^-$$

Oxidation of N*-attached groups:*

Anilines may be oxidized to the corresponding nitrobenzenes by oxidation with peroxytrifluoroacetic acid (a mixture of trifluoroacetic anhydride and hydrogen peroxide).

$$\phi\text{—NH}_2 \xrightarrow{CF_3CO_3H} \phi\text{—NO}_2$$

---

[9] L. Henry, *Compt. rend.* **102**, 1106 (1887).

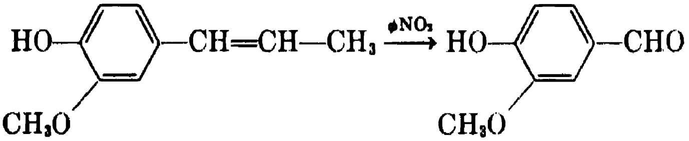
The yields are good, and the method may be used with most substituted anilines. Other N-attached groups, such as nitroso and oximino groups, may be oxidized to nitro groups too, but generalized conditions have not been developed.

2. Chemical properties.

Nitrobenzene is a mild oxidizing agent and may be used to oxidize $\phi\text{—C=C}$ groups to the respective $\phi\text{—C=O}$ groups.

$$\phi\text{—CH=CH—R} + \phi'\text{—NO}_2 \xrightarrow{OH^-} \phi\text{—CHO} + \text{OCH—R} + \phi'\text{—NH}_2$$

For instance, one of the steps in the commercial synthesis of vanillin, an important component of artificial flavors, involves the oxidation of isoeugenol with nitrobenzene.



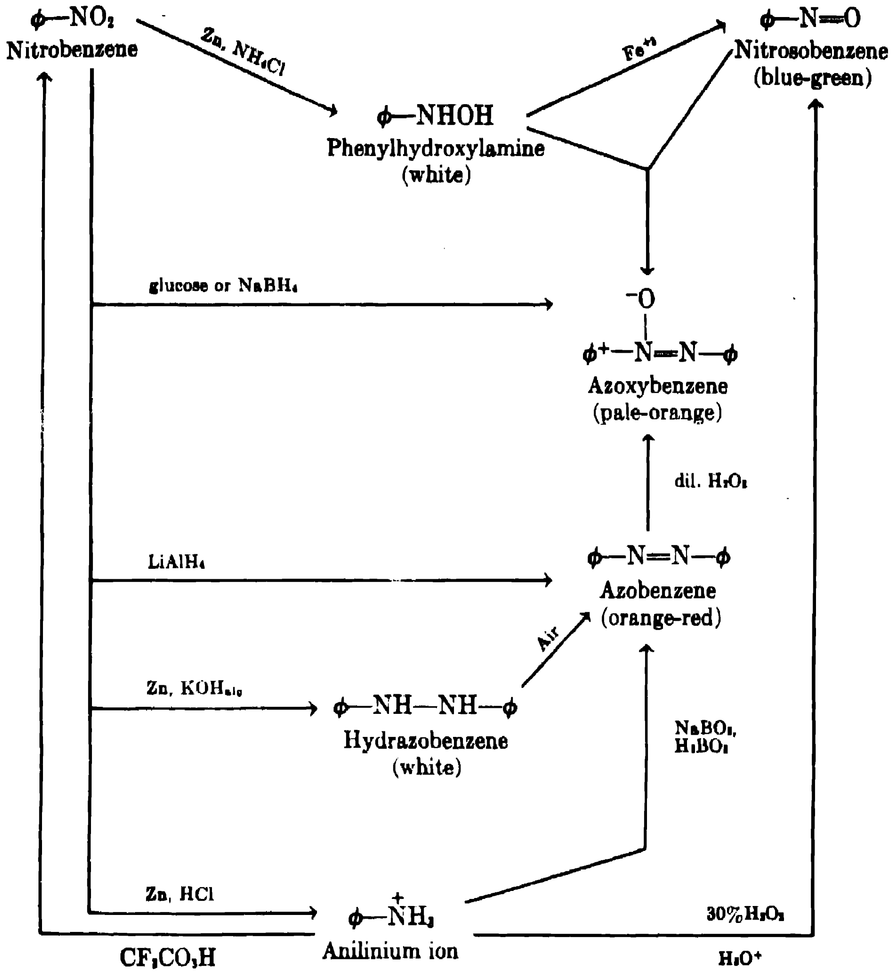
The acid reduction of substituted nitrobenzenes gives the corresponding anilines. This is commonly done with iron, tin, zinc, or stannous chloride.

$$\phi\text{—NO}_2 + \text{Fe} \xrightarrow{H_3O^+} \phi\text{—NH}_3^+$$

The alkaline reduction of nitrobenzene may yield one of several products, depending upon the reducing agent. The successive reduction products and the agents used to produce them are given in Table 16.4. The neutral reduction of nitrobenzene with zinc dust does not stop at the nitrosobenzene stage, although it passes through this stage to the phenylhydroxylamine. When the reduction is carried out in concentrated solutions, some of the nitrosobenzene and phenylhydroxylamine condense to form azoxybenzene. If the latter compound is desired, it can best be made by direct reduction with dextrose or sodium borohydride. Reduction of nitrobenzenes with lithium aluminum hydride yields symmetrical azobenzenes. The preparation of unsymmetrical azobenzenes was given in Section 16.1d.

3. Uses of nitrobenzenes. Because of the activating effect of the nitro group on *ortho-* or *para-*situated halogens, and because of the acid-strengthening effect on *ortho-* or *para-*hydroxyl groups, nitrobenzene derivatives frequently serve as intermediates in organic syntheses. Nitrobenzene is sometimes used as a solvent or mild oxidizing agent. The largest volume use of nitrobenzenes is as explosives. Most of the commercial chemical explosives are polynitro compounds. In general, but not without exceptions, the power of explosives varies indirectly with their sensitivity. There are three broad ranges—high explosives, the boosters, and the detonators. A detonating fuse

TABLE 16.4. REDUCTION STAGES OF NITROBENZENE



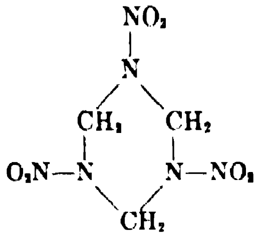
or electric blasting cap is used to set off the booster, whose discharge fires the high explosive. Some of the older explosives are shown in Table 16.5.

TNT is frequently taken as the reference material for explosive power. A modern high explosive used extensively since World War II days is RDX. It is more powerful than TNT, but also more sensitive. A mixture of TNT and RDX is found to form an excellent high explosive. Of course, chemical explosives in the older sense cannot compete with atomic and hydrogen bombs in power, but millions of pounds of chemical explosives are used annually in peacetime, during which time the atomic and hydrogen bombs cannot be used because of the radiation emitted. Industrial explosives are used to remove barriers for the construction of railroads, highways, tunnels, dams, and bridges. Explosives break up valuable ores in mines and rocks in quarries. They blast ditches for drainage, blow out tree stumps rich in turpentine, help

TABLE 16.5. RELATIVE POWER AND SENSITIVITY OF SOME EXPLOSIVE COMPOUNDS

Increasing sensitivity ↓
Increasing power ↑

Compound	Class
Trinitrobenzene (TNB)	High explosives
Ammonium picrate	
Trinitrotoluene (TNT)	
Picric acid	Booster
Lead azide	Detonators
Mercury fulminate	



RDX

excavate foundations for buildings, and open up rivers jammed with logs or ice. In fact, more than a billion pounds of explosives are used annually in the United States.

The Chinese invented gun powder several centuries before the birth of Christ, and it was the only explosive known until Ascanio Sobrero, an Italian professor of chemistry, discovered nitroglycerin (glycerol trinitrate) in 1847.

Nitroglycerin is a very sensitive liquid and too dangerous for practical use. It remained a laboratory curiosity until Alfred Nobel (1833–1896), a Swedish chemist, became interested in it. Nobel invented a detonating device to use nitroglycerin in mines and torpedoes. He obtained patent and manufacturing rights in several countries, but frequent fatal accidents almost caused him to lose his permits to make it or use it. Then, by accident in 1866, he discovered that it could safely be shipped and handled when absorbed by kieselguhr. Nobel called this mixture *dynamite* and patented it in all countries. Although he prospered beyond his wildest dreams, he continued to try to improve it.

One day in 1875 Nobel cut his finger and treated it in the conventional way. He coated the cut with collodion ("new skin"), which left a transparent coating to protect the wound. It occurred to Nobel to try dissolving this highly inflammable material in nitroglycerin to produce a double explosive, but perhaps one less sensitive. This proved to be possible, and the mixture was very insusceptible to shock. Present-day dynamites have some of the nitroglycerin replaced by ethylene glycol dinitrate or ammonium nitrate for safer handling.

Nobel believed that his powerful explosives would prevent war. After several years of debate and thought on war and peace, Nobel provided that the interest from the capital of his estate, nearly 9 million dollars, be distributed in the form of prizes "to those who during the preceding year shall have conferred the greatest benefit on mankind." The five prizes are in the fields of peace, physics, chemistry, physiology and medicine, and literature. These awards are the highest honors that can be conferred on anyone for an outstanding contribution in his profession.

Nobel's dynamite was used successfully in the United States a few years after its discovery. More than 60 million pounds went into the construction of the Panama

Canal after the Americans took over from the French in 1904. Two million pounds were used in constructing Grand Coulee Dam, a structure twice the size of the pyramid of Cheops, which had reigned as man's largest structure for 3000 years. One of the most precise blasting jobs ever performed with dynamite was the damming of Canada's Saguenay River. The river was too deep and flowed too fast to permit construction of a cofferdam in the stream. It was decided to build the dam upright on one side of the river, and tip it in place by blasting. An 11,000-ton reinforced concrete block was built, 92 feet high and 45 feet wide. On July 23, 1930, 1000 pounds of dynamite tipped the huge block, and it splashed into the river within an inch of the calculated position.

One of the key roles played by chemicals in modern space research is as propellants for rocket engines. Here, huge quantities of the chemical reactants (fuel and oxidizer) are converted to hot gases at controlled rates and, when passed through an orifice and subsequently expanded, provide the rocket with forward thrust. Liquid propellants include an oxidizer, such as liquid oxygen, fluorine or nitric acid, and a fuel such as alcohol, kerosene, hydrazine, or liquid hydrogen. For example, in the steering system for the third stage of Saturn V, the launch vehicle for the Apollo manned lunar landing mission, present plans are to use a nitrogen tetroxide-monomethylhydrazine fuel mixture. Solid propellants generally are made by mixing a solid oxidizer such as ammonium salts with a fuel such as nitrocellulose or nitroglycerin together with binders, catalysts, and other ingredients to obtain required characteristics. The solid propellant in the United Aircraft Corporation's 250-ton-weight, million-pound-thrust rocket engine, for example, uses powdered aluminum and ammonium perchlorate in a synthetic rubber bed.

STUDY EXERCISES

1. Illustrate by equations two general methods each of preparing (a) amides, (b) alkyl cyanides, (c) primary nitroalkanes, (d) nitrobenzenes.

2. What reagents and conditions would be used to make the following transformations in the laboratory:

(a) $RNH_2 \rightarrow RNC$
(b) $RCN \rightarrow RCONH_2$
(c) $RNC \rightarrow RNHCH_3$
(d) $RCN \rightarrow R_2CO$
(e) $RNC \rightarrow RNCO$
(f) $RCH_2NO_2 \rightarrow RCHO$
(g) $RCH_2NO_2 \rightarrow RCOOH$
(h) $RCHO \rightarrow RCH(CH_2NO_2)_2$

3. Assign names to the following formulas:

(a) $(C_2H_5)_4NBr$
(b) $(CH_3)_2NC_2H_5$
(c) $C_2H_5NH_3I$
(d) $[(CH_3)_2CH]_3N$
(e) C_2H_5CN
(f) $(i\text{-}C_3H_7)_4NOH$
(g) $CH_3CH_2CH_2CON(CH_3)_2$
(h) $CH_3—CH(NO_2)—CH_3$

4. Complete the following reactions, supplying any reagents or conditions necessary:

(a) $C_2H_5NH_2{:}HCl + NaNO_2 + HCl$
(b) $i\text{-}C_3H_7NH_2 + CHCl_3$
(c) $i\text{-}C_5H_{11}NC + H_2O$
(d) $n\text{-}C_4H_9NC + NaHg$

5. How does the use of the terms *primary*, *secondary*, and *tertiary* differ when applied to amines, alcohols, and nitroalkanes?

6. Write electronic structures for ethyl nitrate, ethyl nitrite, nitroethane, ethyl cyanide, ethyl isocyanide, triethylamine oxide, and tetramethylammonium hydroxide.

7. Give the name and structures of the successive alkaline reduction stages of nitrobenzene, and reducing agents for producing them.

8. What is the structure of RDX?

9. State several uses of substituted nitrobenzenes.

10. How do you account for the fact that N,N-dimethylformamide has a larger molecular weight but boils at a lower temperature (153°) than formamide (193°)?

TEST QUESTIONS, Set 17

1. From the following facts, deduce the structural formula of an unknown compound A:

   (a) From analysis and molecular-weight determination, A is found to have the molecular formula C_3H_7NO.
   (b) Upon hydrolysis of A, an amine B and a carboxylic acid C are isolated.
   (c) B reacts with benzenesulfonyl chloride to give a product insoluble in aqueous alkali.
   (d) C reduces Tollens' reagent.

2. What volume of 2.0 *N* HCl would be necessary to neutralize the amine liberated in the hydrolysis of 25.8 g of N-ethyl-N-methylbutyramide?

3. Predict the relative order of boiling points of acetic acid, acetamide, N-methylacetamide, and N,N-dimethylacetamide. Give the basis for your prediction and compare it with the observed facts.

4. How could the following be distinguished by qualitative test-tube experiments: (a) propionamide from propionitrile, (b) acetamide from ammonium acetate, (c) 1-nitropropane from 2-nitropropane, (d) ethyl isocyanide from ethyl cyanide, (e) ethyl nitrite from nitroethane?

5. Explain the fact that nitromethane does not have a high solubility in hydrocarbons.

6. Predict the better solvent for methylammonium chloride, methanol or propanol, and explain the basis for your prediction.

7. A compound A, $C_6H_{10}O_4$, reacts with sodium metal to liberate hydrogen gas, gives a negative test for a 1,2-glycol, gives a positive iodoform test, does not give a 2,4-dinitrophenylhydrazone, and when reacted with excess acetyl chloride, A gives B, $C_9H_{14}O_6$. When A is refluxed in dilute alkali for one hour and the reaction mixture acidified, two compounds C and D are recovered. C is neutral to litmus and when gently warmed with periodic acid, the mixture gives a white precipitate upon the addition of aqueous silver nitrate. D is acid to litmus, turns ceric ammonium nitrate solution red, gives a positive iodoform test, but gives no 2,4-dinitrophenylhydrazone. What are the structures of A, C, and D? Show how you reached your conclusion.

8. How could one convert $ROOC—CH_2—CH_2—CONH_2$ into $ROOC—CH_2—CH_2—COOH$?

9. Nitrobenzene has a higher boiling point than toluene. Can it be separated from toluene by steam distillation, and why or why not?

10. What weight of iron is required to reduce 1.5 moles of nitrotoluene to toluidine (aminotoluene) in acid solution? Assume that the iron is oxidized to Fe^{+3}.

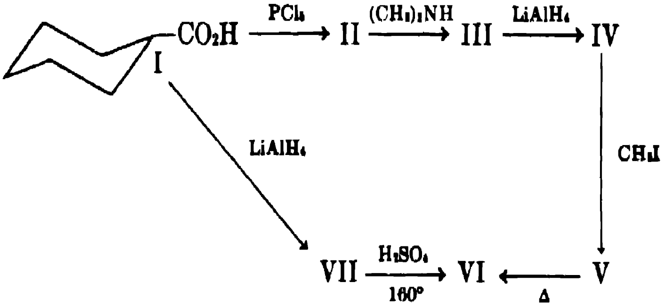
11. Would there be any advantage in using nitrobenzoic acid or nitrobenzenesulfonic acid over using nitrobenzene for the oxidation of substituted styrenes to the corresponding benzaldehydes in aqueous alkali?

12. What series of laboratory reactions would you use to prepare 1,2,3-trinitrobenzene from aniline?

13. Indicate the series of consecutive reactions one could use in the laboratory: to transform

(a) $(CH_3)_2CH{-}CH_2CH_2CH_2OH$ to $(CH_3)_2CH{-}CH_2CH_2CH_2CH_2NO_2$
(b) $CH_3CH_2CH_2CH_2CH_2CO_2C_2H_5$ to $CH_3CH_2CH_2CH_2CN$

14. Give formulas for compounds I–VII formed in the following reaction sequences:



15. (See Section 21.1 for functional group spectral characteristics.) Give possible structures for a compound $C_5H_{11}NO$ (a) if it has infrared bands in the 3300–3400 and 1650 cm^{-1} regions and can be hydrolyzed to diethyl ketone; (b) if it is neutral, has no band in the 3450 cm^{-1} region but has a band at 1663 cm^{-1}; (c) if it is neutral and has doublets in the 3450 and 1650 cm^{-1} regions; or (d) if it is basic but has no band in the 3400 or 1650–1720 cm^{-1} ranges.

17

Optical Activity

17.1 SOME BASIC CHARACTERISTICS OF VISIBLE LIGHT

The regions of the electromagnetic spectrum of interest to a chemist were discussed briefly in Section 6.3. Between the two ranges of ultraviolet and infrared shown in Table 6.3 there is a narrow range called the *visible spectrum* (cf. Section 27.1). In the visible region, the wavelength of light determines its color, and ordinary white light is light of all wavelengths within this range. Prisms have the ability to break up a light beam into its various colors; and, if a slit is placed at various positions behind the prism, a light ray of one color called *monochromatic light* is obtained.

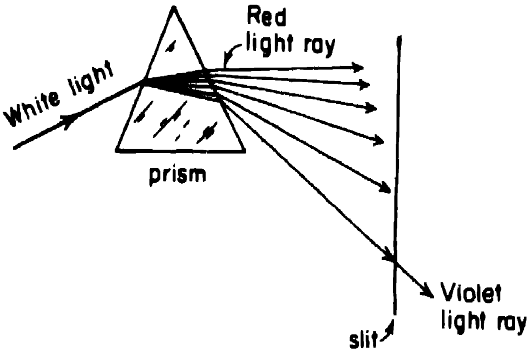


Fig. 17.1.

When looking at a wave motion from the front, one sees only the vertical motion. Light waves vibrate in planes in any orientation, and ordinary light has rays vibrating in all orientations with respect to the earth. When coming

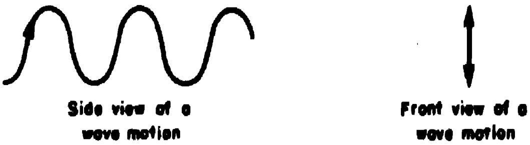


Fig. 17.2.

into the eye, daylight has planes of vibration at all angles within 360°. When such a beam of light passes through a crystal of calcite ($CaCO_3$) or quartz (SiO_2), the crystal will transmit only two rays of light whose planes of vibration are perpendicular to each other.

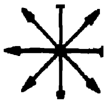


Fig. 17.3. Planes of vibration of daylight entering the eye.

This is called *double refraction*, because a single line viewed through the crystal appears as two lines. When a beam of ordinary light is passed through a crystal of tourmaline (a complex aluminum-boron silicate), the component vibrating in one plane is absorbed more strongly than that vibrating perpendicular to this plane. This phenomenon is called *dichroism*. Tourmaline crystals, if thick enough, may completely absorb one component, and the transmitted light will be polarized. By making a film of properly oriented microscopic crystals of a dichroic substance (such as quinine periodide sulfate), large plates may be manufactured which transmit partially polarized light. These are used for eyeglasses and car headlight lenses, since polarized light gives off little glare.

If a crystal of calcite is split along one of its natural axes, and then the two halves are cemented together with Canada balsam, the emerging ray of light will be vibrating in only one plane. The split crystal is called a Nicol prism; and light, whose vibrations are in one plane, is called *polarized light*. Hence, one may produce with the use of natural or Nicol prisms, either polarized or nonpolarized monochromatic light, and also polarized or nonpolarized white light.

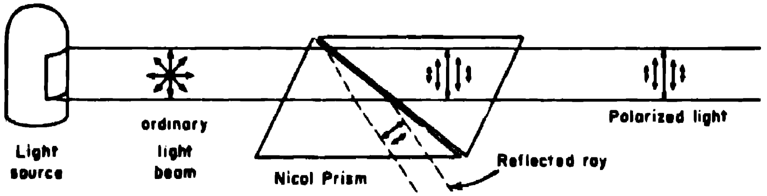


Fig. 17.4.

In order to ascertain the plane of polarization of a polarized light beam, one uses two Nicol prisms; the apparatus is called a *polariscope* or *polarimeter*. When the polarized beam from one Nicol prism enters a second Nicol prism, and if the second prism is oriented at the proper angle, most of the light beam will pass right through. On the other hand, if the second prism is turned 90° to this proper angle, no light will pass through.

A crude analogy has been given as follows. Have a score or so of ropes tied to separate hooks in a horizontal row on a wall, and have a line of people each holding the end of a rope about 20 feet away from the wall. Now, have the people shake the ropes back and forth, some vertically, some horizontally, and some at various oblique angles. This will set up waves in the ropes similar to light waves.

Next, a picket fence with vertical pickets is dropped about one-third the distance from the people to the wall, and it will be seen that only those waves vibrating nearly parallel to the pickets will pass through. The other waves are stopped by the fence. This simulates plane polarized light.

Then, a second picket fence is dropped midway between the first fence and the wall, and it will be seen that the waves also pass through the second fence. However, if the second fence is tipped over slowly to one side, fewer and fewer waves pass through the second fence until, at right angles, all waves will be stopped. This simulates crossed Nicol prisms, which transmit no light.

The angle at which the second prism has to be set in order to transmit the maximum amount of light reveals the plane of polarization of the light transmitted by the first Nicol prism.

Now, it is found that certain substances in the crystalline state or in solution possess the ability of changing the plane of vibration of a polarized light beam when the light passes through these substances. Such substances are referred to as being optically active. First, the two Nicol prisms are set at an angle at which the maximum intensity of light is seen through the second prism (the *analyzer*). Then, when a solution of the optically active substance is placed between the prisms, the analyzer has to be rotated clockwise (right) or counterclockwise (left) in order to see the maximum amount of light again. The angle through which the analyzer has been turned indicates the *angle of rotation*. Substances which rotate the plane of polarization to the right are called *dextrorotatory*, and those which rotate it to the left are called *levorotatory*. Since the degree of rotation depends on how many optically active molecules the light beam encounters, the angle of rotation is dependent on the length of the light path through the solution, the concentration, the temperature, and also the wavelength of light used. In order to be able to compare measurements by different persons, specific rotations $[\alpha]$ or molecular rotations are computed,

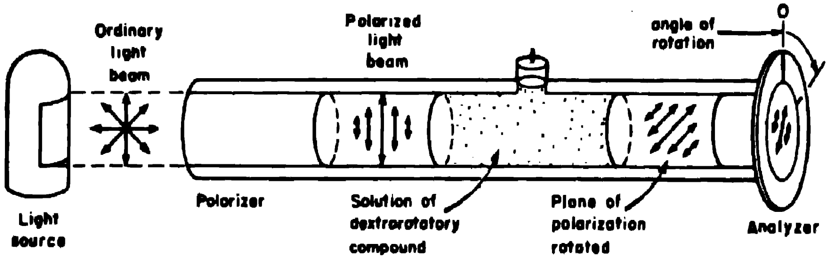


Fig. 17.5. Schematic diagram of a polarimeter.

$$[\alpha] = \frac{\text{angle of rotation (degrees)}}{l\ (\text{dm}) \times c\ (\text{g/cc})}$$

where l is the length of tube in decimeters, and c is the concentration in grams per cubic centimeter. Thus, the *specific rotation* is the rotation produced by a solution containing 1 g/cc in a tube 1 dm long. The *molecular rotation* is the product of the specific rotation by the molecular weight.[1] For illustration, the symbol $[\alpha]_D^{25°} = -66°$ means that the specific rotation of a compound at 25° with sodium vapor light (obtainable with a Bunsen burner when the air is drawn through a sodium salt solution) is 66 degrees to the left (counterclockwise).

17.2 OPTICAL ISOMERISM

It was stated in Section 1.6 that whenever four different atoms or groups are attached to a single carbon atom, there will be two possible arrangements for the four groups about the carbon atom. The two arrangements give rise to two structures which are the inverted images of each other, or *mirror images* of each other (see page 48). The two molecules have essentially the same physical and chemical properties except for their effect upon polarized light. One will be dextrorotatory and one levorotatory, with equal but opposite rotatory powers. They are isomers, of course, and so they are called *optical isomers, optical antipodes,* or *enantiomorphs* (Gr. *enantios,* opposite, and *morphe,* form). Some properties of several groups of geometric and optical isomers are given in Tables 17.1 and 17.2, from which it may be seen that the physical properties of two optical isomers are virtually the same.

A solution made up of the *dextro* isomer will be dextrorotatory, and a solution of the *levo* isomer will be levorotatory, but a solution of equal molecular amounts of the two isomers will be optically inactive, because the opposing effects of the two types of molecules cancel each other. Such a mixture is called a *racemic mixture,* i.e., an equimolar mixture of two optical isomers.

Carbon atoms having four different atoms or groups attached to them have no plane of symmetry and are therefore asymmetric. Even the molecule R_1R_2CHD, in which the asymmetry of the carbon atom is due to two isotopes, will be optically active although its molecular rotation will be small. Molecules having an asymmetric carbon atom will lack a plane of symmetry and will be optically active. The criterion for determining whether or not a molecule will be optically active is the lack or presence of a plane of symmetry.[2]

To understand why asymmetry leads to optical isomerism, two logical points must be accepted. (1) In a gaseous or liquid state, molecules are randomly oriented in space. This means that no matter which direction a molecule is oriented in space, there will be one having exactly the opposite orientation. It is unlikely that they will be directly face to face, but merely oppositely oriented somewhere within the sample. (2) The polarizing effect that a molecule has on a light beam is reversed when the molecule takes an opposite orientation with respect to the light beam.

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[1] Following a suggestion of van't Hoff, some chemists divide this molecular rotation by 100.

[2] The lack of a plane of symmetry is not the ultimate criterion (G. E. McCasland and S. P. Proskow, *J. Amer. Chem. Soc.*, **78**, 5646 (1956)). A compound was synthesized which lacks a plane or center of symmetry, but because of its unusual spatial shape, is superposable upon its mirror image. Therefore, it is not optically active. In view of the fact that such cases will be extremely rare, the criterion adopted above will be adequate for this study.

TABLE 17.1. SOME PHYSICAL PROPERTIES OF GEOMETRIC ISOMERS

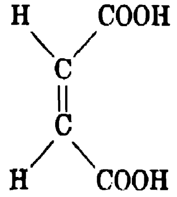
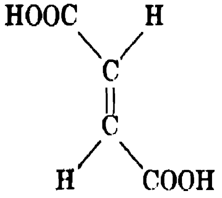
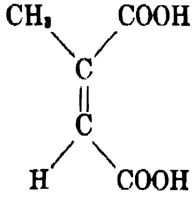
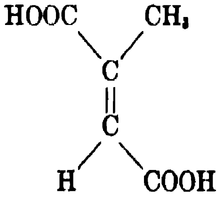
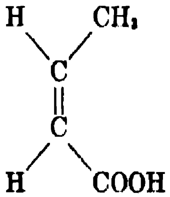
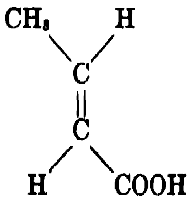
Geometric Isomers		M.P.	Solubility 25°, g./100 g. H_2O
Maleic acid		130.5°	79
Fumaric acid		287	0.7
Citraconic acid		91	
Mesaconic acid		202	
Isocrotonic acid		15.5	40.0
Crotonic acid		72	8.3

TABLE 17.1. Continued

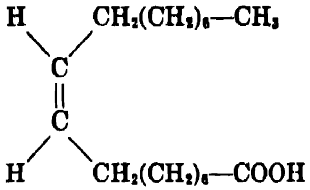
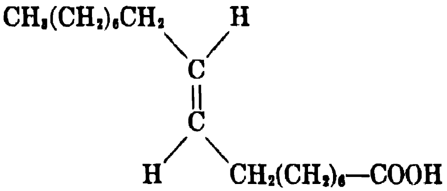
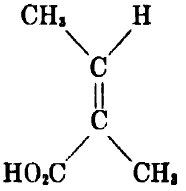
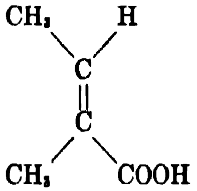
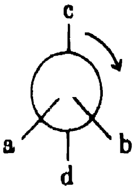
Geometric Isomers		M.P.	Solubility 25°, g./100 g. H_2O
Oleic acid		13°	
Elaidic acid		44	
Angelic acid		45	
Tiglic acid		64.5	

TABLE 17.2. SOME PHYSICAL PROPERTIES OF OPTICAL ISOMERS

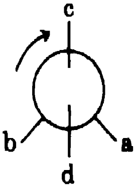
$C_6H_5CH(OH)COOH$, Mandelic Acid				
	M.P.	Solubility 25°, g./100 g. H_2O	pK_a	$[\alpha]^{20°}_D$
Dextro	132.8°	8.54		+155.5°
Levo	132.8	8.64	3.37	−154.4
Racemic mixture	118.5	15.97	3.38	0
$CH_3CH(OH)COOH$, Lactic Acid				
Dextro	26°	∞		+2.24°
Levo	26	∞		−2.24
Racemic mixture	18	∞		0

Atoms are merely ordered arrangements of charged particles and, owing to the electrical character of light, it is to be expected that there should be some kind of interaction when a light beam passes an atom or molecule. This is indeed the case. Every molecule is affected by, and affects, a passing light beam. Two identical molecules, of course, have identical effects. Each atom in a molecule has some attraction or repulsion for the light beam, so that after a polarized light ray has passed an asymmetric molecule, its original plane of polarization is rotated through some angle. If the molecule is facing just the opposite direction, its rotatory power is reversed.

For illustration, suppose the following molecule



rotates a beam from c toward b, i.e., clockwise here. Then, when it is turned to face the opposite direction,



it will rotate the plane of polarization from b toward c. However, this is still clockwise with respect to the same light beam. Hence, no matter which way the asymmetric molecule is facing with respect to the light beam, it will rotate the plane of polarization in the same direction. Therefore, *a solution made up of identical asymmetric molecules will be optically active.*

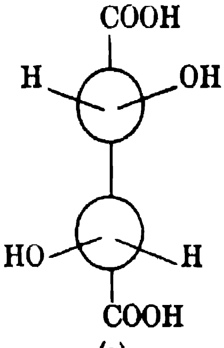
Obviously, two molecules which are mirror images have opposite effects upon a light beam when facing the same direction. Now, it was just shown that when an asymmetric molecule reverses its direction, it still rotates a polarized beam in the same clockwise or counterclockwise direction with respect to the light beam. Therefore, *a solution made up of molecules which are mirror images will be optically inactive*, because each isomer will have an identical molecule facing the opposite direction; and the two pairs of identical molecules will rotate the plane of polarization in opposite directions, thereby nullifying the effect of each pair.

With models, it may be seen that if there are two identical atoms or groups attached to a carbon atom, i.e., the carbon atom is not asymmetric, two such molecules will be *identical* as well as *mirror images*. Hence, as deduced above, a solution made up of molecules that are mirror images will be optically inactive, although they may also be identical.

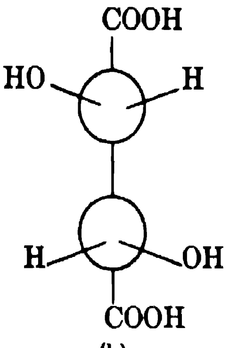
17.3 NUMBERS OF OPTICAL ISOMERS

If a molecule has more than one asymmetric carbon atom, then more than two optically active isomers are possible. For illustration, consider the classic case of tartaric acid, HOOC—CHOH—CHOH—COOH. The two center carbons each contain four different atoms or groups attached thereto (an H atom, an OH, a COOH, and the complex group —CHOH—COOH); hence, they are each asymmetric. This allows two independent arrangements of the four groups about each carbon atom, making each have a dextrorotatory and a levorotatory effect. Now, let us see how many isomeric molecules may arise.

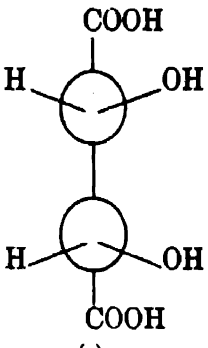
Using models, one finds there are three different isomers possible which can be diagramed as follows. The circles represent carbon atoms. Bonds extending into the circles point forward, and those just touching the circles point backward.



(a)



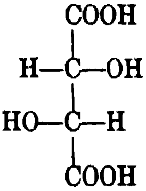
(b)



(c)

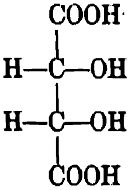
It is seen that (a) and (b) are mirror images of each other, that the top half of (c) is identical to either half of (a), and the lower half of (c) is identical to either half of (b). Also, one-half of (c) is a mirror image of the other half.

Unless models are used, or unless formulas as above are used to indicate the three-dimensional shape of the molecules, it might not be evident that (a) and (b) are different from (c). That is, if the usual projection formulas are used,



$$\begin{array}{c} \mathrm{COOH} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{HO{-}C{-}H} \\ | \\ \mathrm{COOH} \end{array}$$

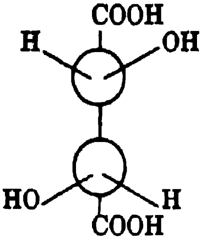
(a)



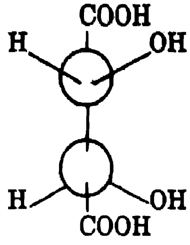
$$\begin{array}{c} \mathrm{COOH} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{COOH} \end{array}$$

(c)

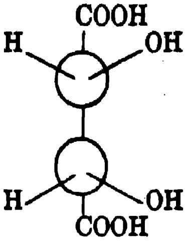
the student might ask, "Because of free rotation, when the lower half of (a) rotates 180° about the center C—C bond, does it not become (c)?" This would appear to be the case from the projection formulas, but with models or the diagrams above, it will be found that if the rotation does occur, the molecules are still not identical. The COOH group in (a) extends backward, and after rotation occurs, it would point forward. It can be seen, then, that (a) and (c) still would not fit the same mold, i.e., are not identical.



(a)



Structure of (a) after 180° rotation of lower group about center C—C bond.



(c)

However, are all three isomers optically active? An answer to this question may be found as follows. Name the atoms or groups as one goes around each asymmetric carbon atom of the projection formula in a clockwise direction, starting any place. For (a) the order is OH, G, H, COOH, OH, G, H, etc., for both asymmetric carbon atoms, where G stands for the complex group —CHOH—COOH. For (b) it is OH, COOH, H, G, OH, COOH, etc., around each asymmetric carbon atom. Note that these two sequences are exactly opposite. Hence, the rotatory power of each asymmetric carbon in (a) is the same, and that of each asymmetric carbon in (b) is the same. Thus, the rotatory effect of each half of (a) is the same, making the entire molecule optically active. The same is true for (b), but its optical activity will be equal and opposite to that of (a). The two isomers, being mirror images, are optically active in equal but opposite directions.

When the same analysis is made for (c), the top asymmetric carbon has the sequence, OH, G, H, COOH, OH, G, H, etc., while the bottom asymmetric carbon has the order, OH, COOH, H, G, OH, COOH, etc. These two orders are exactly opposite, making the two asymmetric carbons have equal but opposite rotatory powers. The effect of each cancels the effect of the other, making the molecule optically inactive. This will always be the case when one-half of a molecule is the mirror image of the other half. Such isomers are called *meso* isomers, and, although within them there are asymmetric carbon atoms, they are optically inactive due to *internal compensation;* i.e., the optical effect of each half cancels that of the other half.

TABLE 17.3. PROPERTIES OF THE ISOMERS AND *DL* RACEMATE OF TARTARIC ACID

	M.p.	Density	Solubility g./100 g.H_2O	Acid Dissociation		$[\alpha]_D^{20°}$
				pK_1	pK_2	
d-Tartaric acid	170°	1.76	139	2.93	4.23	+12°
l-Tartaric acid	170	1.76	139	2.93	4.23	−12°
meso-Tartaric acid	140	1.67	125	3.11	4.80	0
dl-Tartaric acid	206	1.70	20.6	2.96	4.24	0

Therefore, there are three isomers of tartaric acid: two optically active and one optically inactive. Some properties of the three isomers and of the *dl* racemate are given in Table 17.3.

An analysis as was just made for tartaric acid could be made for all formulas having more than one asymmetric carbon atom, but this would be slow and bothersome. For convenience, there are mathematical formulas by which chemists may calculate the number of isomers for a given projection formula. For aliphatic compounds where the asymmetric carbon atoms are in the main chain, the formulas are as follows. Let

a = the number of optically active isomers
m = the number of optically inactive isomers, i.e., meso isomers
n = the number of asymmetric carbon atoms
r = the number of racemic mixtures $= a/2$ always.

There are three cases or situations which may arise.

Case 1: If the molecule cannot be divided into halves which are mirror images of each other, then $a = 2^n$; $m = 0$.

Case 2: If the molecule can be divided into halves which are mirror images of each other and n is even, then $a = 2^{n-1}$; $m = 2^{(n/2)-1}$.

Case 3: Same as Case 2, except n is odd; i.e., the molecule is divided through the center carbon atom. This atom is called a *pseudo asymmetric carbon atom*, for its asymmetry depends on whether the configurations of the two halves are superposable or not. However, it is included in the number n, and $a = 2^{n-1} - 2^{(n-1)/2}$; $m = 2^{(n-1)/2}$.

For illustration, in the formula $CH_2OH—CHOH—CHOH—CHOH—COOH$, the molecule cannot be divided into mirror-image halves; hence, it falls under Case 1. The three center carbons are asymmetric; therefore, $a = 2^3 = 8$; $m = 0$; $r = a/2 = 4$. In the formula $CH_2OH—CHBr—CHOH—CHOH—CHBr—CH_2OH$, one-half of the molecule can be a mirror image of the other half; i.e., one could fold the molecule in half, and one-half would fit on top of the other half. Since the number of asymmetric carbon atoms is even (4), this falls in Case 2. Hence, $a = 2^{4-1} = 2^3 = 8$; $m = 2^{(4/2)-1} = 2^{2-1} = 2$; $r = a/2 = 4$.

In the formula, $HOOC—CH(CH_3)—CHOH—CHBr—CHOH—CH(CH_3)—COOH$, again the molecule may be folded through the center having one-half fit on top of the other half. Since the number of asymmetric carbon atoms is odd (5), this falls in Case 3. Hence, $a = 2^{5-1} - 2^{(5-1)/2} = 2^4 - 2^2 = 16 - 4 = 12$; $m = 2^{(5-1)/2} = 2^2 = 4$; $r = a/2 = 6$.

17.4 RACEMIZATION

Molecules often undergo inversions during reactions, particularly during nucleophilic displacement reactions (page 230), but unless the molecules are optically active, one is not aware of any inversions having occurred. When a *dextro* isomer inverts, it becomes the *levo* isomer, and conversely. Thus, the inversions are easily detectable for asymmetric molecules.

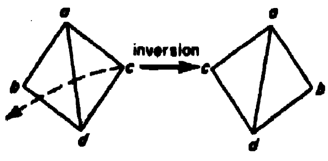


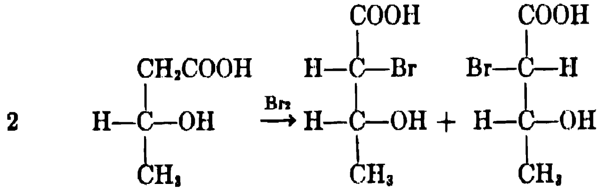
Fig. 17.6.

When an optically active substance is heated in solution, particularly acids in alkaline media, inversions take place back and forth until equal amounts of the two isomers are present. Thus, an optically active sample becomes a racemic mixture. This process is called *racemization*, and the mixture of optically active isomers is called a racemic mixture or racemate.

17.5 RESOLUTION OF RACEMIC MIXTURES

The process opposite to racemization, resolution of a racemic mixture, is more important. In a chemical synthesis, ordinarily, a racemic mixture is obtained. In most reactions, both isomers have the same chance of being formed; so they are formed in equal amounts.

The synthesis of only one of a pair of optical antipodes, called asymmetric synthesis or asymmetric induction, can be accomplished to give partially optically pure compounds. Nevertheless, all useful methods discovered so far require previously prepared optically active substances somewhere in the synthesis. For example, the reduction of ketones by asymmetric Grignard reagents[1] or with aluminum alkoxide in an optically active alcohol solvent[2] yields an optically active alcohol from the ketone. Another method is to produce a new asymmetric carbon atom in an optically active compound and separate the arising diastereoisomers by fractionation. For illustration,



$$2\ \begin{array}{c} CH_2COOH \\ | \\ H{-}C{-}OH \\ | \\ CH_3 \end{array} \xrightarrow{Br_2} \begin{array}{c} COOH \\ | \\ H{-}C{-}Br \\ | \\ H{-}C{-}OH \\ | \\ CH_3 \end{array} + \begin{array}{c} COOH \\ | \\ Br{-}C{-}H \\ | \\ H{-}C{-}OH \\ | \\ CH_3 \end{array}$$

l-β-Hydroxy-butyric acid

Diastereoisomers (separable by fractional crystallization)

Also, by irradiating a *dl*-mixture with *dextro* circularly polarized light, it is possible to cause one isomer to decompose more rapidly than the other, thereby enriching the mixture with respect to the more stable isomer.

Since most biological reactions involving asymmetric molecules are concerned with only one of the possible optical antipodes, biological syntheses produce optically active materials. It is not uncommon, then, to employ plants, yeast, or other living systems for synthesizing optically active substances. For example, D-lactic acid is produced commercially by the selective reduction of pyruvic acid, $CH_3{-}CO{-}COOH$, with *Bacillus delbruckii*.

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[1] H. S. Mosher and E. LaCombe, *J. Am. Chem. Soc.* **72**, 3994 (1950).

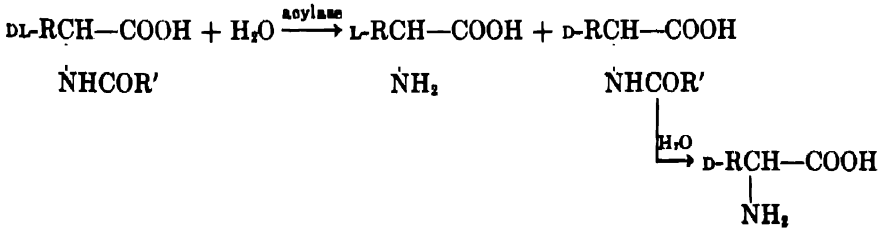
[2] W. E. Doering and R. W. Young, *ibid.* **72**, 631 (1950).

It so happens that most physiologically active substances (drugs and medicinals) involve optically active substances, and only one isomer will be effective. Hence, racemic mixtures need to be resolved in order to get the drug of greater potency. Also, for a number of theoretical studies and for chemical synthesis, it is important to resolve racemates in order to isolate the pure optically active isomers.

It was Louis Pasteur who first reported successful resolutions of racemic mixtures, and it is a tribute to him that his three methods of resolution remained the sole methods in general use for almost a century.

His first method resulted from his keen observation that when tartaric acid is allowed to crystallize slowly from a dilute, cool solution, the crystals are of two shapes which are mirror images of each other. Pasteur separated the two types of crystals by hand, and he found that solutions made up separately from the two batches were identical, except that they rotated the plane of polarization of polarized light to the same extent in opposite directions. This method of resolution, referred to as the *mechanical method*, is obviously impractical, because (1) often substances do not crystallize into readily distinguishable crystals, (2) such a separation would be very slow, and (3) it cannot be used for liquid substances. An unusual case was reported in which a *dl*-mixture was allowed to crystallize very slowly to produce large, easily distinguishable crystals (one weighing 11 g).[3]

A second method of resolution, sometimes called the *biochemical method*, employs living organisms to destroy or metabolize one optical isomer. Pasteur in 1858 found that *d*-ammonium tartrate is destroyed more rapidly than the *l*-form by *Penicillum glaucum*. Similarly, Fischer found in 1898 that D-glucose can be fermented by yeast, but L-glucose is unaffected. This method, then, depends upon finding an organism that will destroy the undesired optical isomer, and such a fortuitous discovery may not occur in one's lifetime. For this reason, and because one isomer is destroyed by the organism, the method does not offer a wide generality. A very useful application of this technique, however, has been developed for amino acids. An amino acid racemate is acylated, then hydrolyzed with an enzyme (acylase or amidase) which selectively catalyzes the cleavage of amide groups of L isomers. The hydrolyzed L amino acid is easily separated from the acylated D amino acid, and then the latter is hydrolyzed separately to yield the D amino acid.



$$\text{DL-}\underset{\text{NHCOR}'}{\text{RCH}}\text{—COOH} + H_2O \xrightarrow{\text{acylase}} \text{L-}\underset{\text{NH}_2}{\text{RCH}}\text{—COOH} + \text{D-}\underset{\text{NHCOR}'}{\text{RCH}}\text{—COOH} \xrightarrow{H_2O} \text{D-}\underset{\text{NH}_2}{\text{RCH}}\text{—COOH}$$

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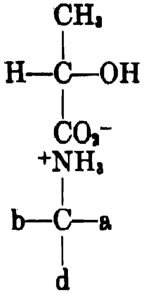
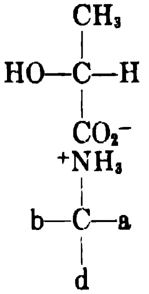
[3] H. E. Zaugg, *J. Am. Chem. Soc.* 77, 2910 (1955).

Pasteur's third method, called the chemical method or, more appropriately, the *diastereoisomer fractionation method*, finds the widest utilization. This method employs an acid or base already available in either a *d*- or *l*-form. Upon reaction with a *dl*-acid, for example, a *d'*-base will produce two salts. The one with the *d*-acid can be designated *dd'*-salt, and the one with the *l*-acid, an *ld'*-salt. These two salts will not be mirror images. Actually, parts of each salt are identical, and parts of each salt are mirror images.



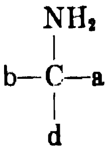
$$\begin{array}{c} CH_3 \\ | \\ H\text{—}C\text{—}OH \\ | \\ CO_2^- \\ {}^+NH_3 \\ | \\ b\text{—}C\text{—}a \\ | \\ d \end{array}$$

l-Amine salt of *l*-lactic acid



$$\begin{array}{c} CH_3 \\ | \\ HO\text{—}C\text{—}H \\ | \\ CO_2^- \\ {}^+NH_3 \\ | \\ b\text{—}C\text{—}a \\ | \\ d \end{array}$$

l-Amine salt of *d*-lactic acid

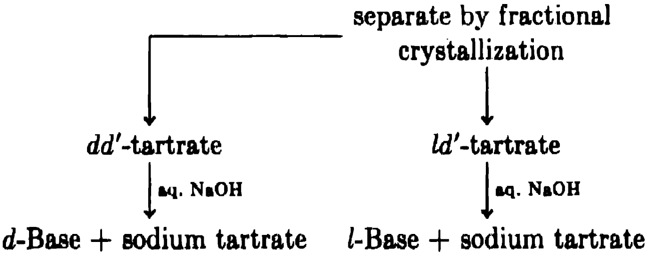


$$\begin{array}{c} NH_2 \\ | \\ b\text{—}C\text{—}a \\ | \\ d \end{array}$$

Represents an *l*-amine, and $CH_3CHOH\text{—}COOH$ is lactic acid

Two molecules having some parts identical and other parts mirror images are called *diastereoisomers*. Not being completely mirror images, they have different physical properties, including different solubilities. They may, therefore, be separated by fractional crystallization. After the salts have been separated, the original organic optical isomeric acids (or bases) may be recovered by the addition of mineral acid (or base). For illustration, to separate a racemic mixture of an organic base, one could use either *d*- or *l*-tartaric acid.

dl-base + *d'*-tartaric acid → *dd'*-tartrate + *ld'*-tartrate



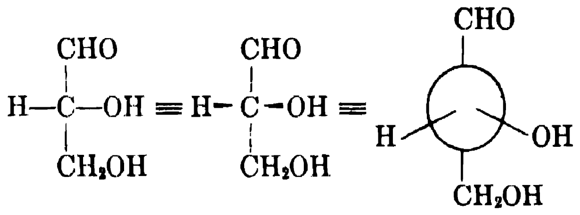
If the organic bases do not separate from the aqueous phase, they may be isolated by ether or chloroform extraction. For a specific example, the potent analgesic *l*-methadone has been separated from the almost ineffective *d*-isomer by crystallization of the *d*-tartrate from acetone, or by neutralization with *d*-α-bromocamphor-sulfonic acid which forms a water-insoluble salt with *d*-methadone and a water-soluble salt with the *l*-isomer.

For racemates other than acids or bases, other types of diastereoisomeric compounds can be formed and fractionated. For instance, alcohols may be esterified with optically active acids to yield solid esters. After the esters have been fractionated, the active alcohols are recovered by separate hydrolysis of the esters. Hydrolysis does not racemize the alcohol.

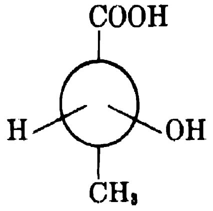
In recent years, resolutions of racemic mixtures have been achieved by adsorption on crystal surfaces of quartz, or on adsorption columns containing optically active adsorbents. A more recent method involves the formation of *inclusion complexes* (page 470). When certain substances crystallize in the presence of certain other compounds, the crystals envelop the foreign molecules in the open crystal cavities, and such crystalline mixtures are called *inclusion complexes*. Occasionally, the crystallizing molecules selectively occlude one isomer of a racemic mixture, thereby affecting a resolution.

17.6 ABSOLUTE AND RELATIVE CONFIGURATIONS

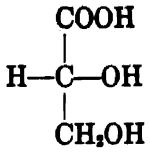
At one time it was impossible to say just which of the two formulas of lactic acid corresponds to that of the *dextro* isomer; that is, one could not assign the absolute configuration of an optically active molecule. However, if the configuration of some reference compound were *arbitrarily assumed*, then chemists could relate the configuration of other active compounds to this reference substance and to each other. These would be called *relative configurations*. In 1908, Emil Fischer proposed the structure of D-glyceraldehyde to be as follows:



The *dextro* isomer has the H and OH forward, and the CHO and CH_2OH group extend backward. This convention is widely accepted, and compounds related to D-glyceraldehyde with respect to the orientation of H and OH are termed D-isomers, irrespective of whether they happen to be dextro- or levorotatory. Thus, the related lactic acid,

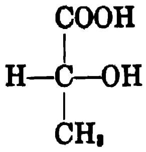


is levorotatory and is named D(−)-lactic acid. The stereo relation to glyceraldehyde is indicated by a small capital D or L, while the actual direction of optical rotation is indicated by a plus or minus sign in parentheses.



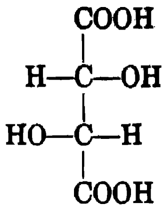
$$\begin{array}{c} COOH \\ | \\ H-C-OH \\ | \\ CH_2OH \end{array}$$

D(−)-Glyceric acid



$$\begin{array}{c} COOH \\ | \\ H-C-OH \\ | \\ CH_3 \end{array}$$

D(−)-Lactic acid



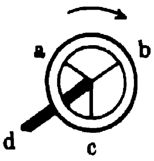
$$\begin{array}{c} COOH \\ | \\ H-C-OH \\ | \\ HO-C-H \\ | \\ COOH \end{array}$$

L(+)-Tartaric acid

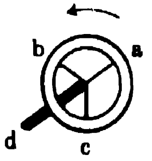
Compounds whose structures bear no relation to glyceraldehyde, such as alkaloids, merely use the lower case *d* and *l* to indicate their direction of optical activity.

In 1951 a technique was developed for X-ray diffraction analysis whereby the absolute configuration of a molecule may be determined[4] and indeed, it was found that D(+)-glyceraldehyde actually has the structure assigned to it by Fischer. The absolute configuration of other types of compounds are now known too, and this has made it necessary to have a method of describing the configuration of the atoms in a molecule. Of the various proposed schemes, that which is generally adopted now is the R-S configurational nomenclature.[5]

R-S configurational nomenclature. This system uses the letters R (for *rectus*, Latin for right) and S (for *sinister*, Latin for left). To indicate the structure about an asymmetric atom X in X_{abcd}, the groups a, b, c, and d are arranged in a priority sequence based on the *sequence rule* stated below. Then the grouping is viewed from the side remote from d, which is referred to as the "steering wheel" model. If the sequence a, b, c, is in a clockwise rotation, the arrangement is designated R, whereas the opposite rotation is called S.



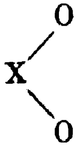
R



S

The Sequence Rule

1. Groups attached to the asymmetric atom are listed in order of decreasing atomic weight, for identical α atoms, then in order of decreasing atomic weights of β, γ, etc., until a sequence is obtained.
2. Substitute an equal number of identical atoms for multiple bonds, e.g.,



$$\begin{array}{l} \quad O \\ \ / \\ X \\ \ \backslash \\ \quad O \end{array}$$

for X=O.

---

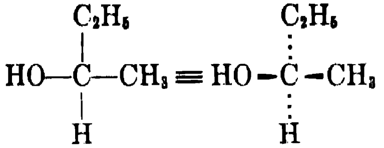
[4] J. M. Bijoet, *Endeavour*, April 1955, p. 71.

[5] Cf. R. S. Cahn, *J. Chem. Educ.*, **41**, 116 (1964).

3. **Isotopic atoms of higher mass number precede those of lower mass number, e.g., X_{aTDH} for tritium, deuterium, and hydrogen.**
4. ***Cis* groups precede isomeric *trans* groups, and R groups precede isomeric S groups.**

These rules give the following order of decreasing priority for some common groups: I, Br, Cl, SH, F, OCOR, OR, OH, NO_2, NHCOR, NR_2, NH_2, COCl, CO_2R, CO_2H, $CONH_2$, COR, CHO, CH_2OH, C_6H_5, CR_3, CHR_2, CH_2R, CH_3, D, H.

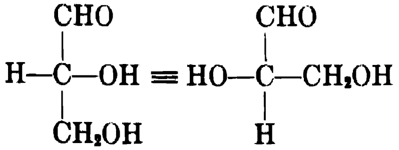
The procedure for naming compounds is illustrated by the following examples:



$$\begin{array}{c} C_2H_5 \\ | \\ HO{-}C{-}CH_3 \\ | \\ H \end{array} \equiv \begin{array}{c} C_2H_5 \\ \vdots \\ HO - C - CH_3 \\ \vdots \\ H \end{array}$$

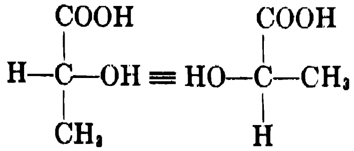
Sequence rule = HO, C_2H_5, CH_3, H
a b c d
= R

It is often convenient to use a Fischer projection formula, in which case the groups are moved about by an even number of exchanged pairs of groups until group d occupies the bottom position. Then the groups are read off to ascertain the rotation of a, b, c. If this is done for D-glyceraldehyde, for instance, we get R-glyceraldehyde by two exchanges: H for CH_2OH, then any other couple excluding H:



$$\begin{array}{c} CHO \\ | \\ H{-}C{-}OH \\ | \\ CH_2OH \end{array} \equiv \begin{array}{c} CHO \\ | \\ HO{-}C{-}CH_2OH \\ | \\ H \end{array}$$

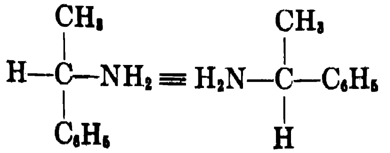
Sequence rule = HO, CHO, CH_2OH, H
a b c d
= R



$$\begin{array}{c} COOH \\ | \\ H{-}C{-}OH \\ | \\ CH_3 \end{array} \equiv \begin{array}{c} COOH \\ | \\ HO{-}C{-}CH_3 \\ | \\ H \end{array}$$

R(−)-Lactic acid

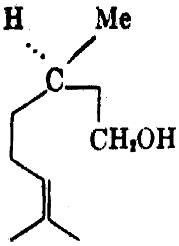
Sequence rule = OH, COOH, CH_3, H
a b c d
= R



$$\begin{array}{c} CH_3 \\ | \\ H{-}C{-}NH_2 \\ | \\ C_6H_5 \end{array} \equiv \begin{array}{c} CH_3 \\ | \\ H_2N{-}C{-}C_6H_5 \\ | \\ H \end{array}$$

(S)-α-Phenylethylamine

Sequence rule = NH_2, C_6H_5, CH_3, H
a b c d
= S

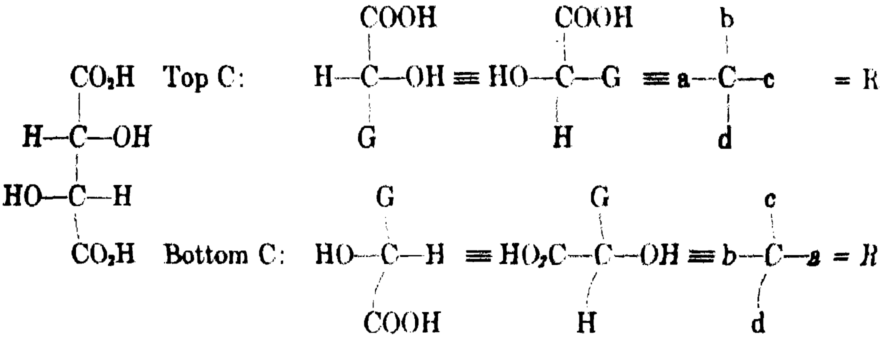


3(R)-Methyl-7-methyl-6-octenol

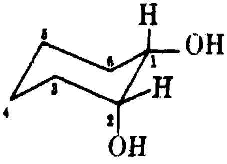
Sequence rule = $\underset{a}{CH_2CH_2OH}$, $\underset{b}{CH_2CH_2C{=}CMe_2}$, $\underset{c}{CH_3}$, $\underset{d}{H}$

According to steering wheel model, this is R.

When there is more than one asymmetric atom, a symbol is attached to each:


CO_2H
H—C—OH
HO—C—H
CO_2H
Top C:
COOH
H—C—OH ≡ HO—C—G ≡ a—C—c = R
G
H
b
d
Bottom C:
G
HO—C—H ≡ HO_2C—C—OH ≡ b—C—a = R
COOH
H
c
d

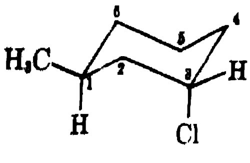
∴ Name = 2(R),3(R)-Dihydroxysuccinic acid, or (R)-(+)-tartaric acid.



Sequence rule for C_1 = OH, C_2, C_6, H
Steering wheel model gives S.

Sequence rule for C_2 = OH, C_1, C_3, H
Steering wheel model gives R.

∴ Name = 1(S),2(R)-Cyclohexanediol.



Sequence rule for C_1 = C_2, C_6, CH_3, H
Steering wheel model gives S.

Sequence rule for C_3 = Cl, C_2, C_4, H
Steering wheel model gives S.

Name = 1(S)-Methyl-3(S)-chlorocyclohexane

STUDY EXERCISES

1. Define or explain the following terms: (a) monochromatic light, (b) polarized light, (c) polariscope, (d) specific rotation, (e) molar rotation, (f) diastereoisomer, (g) optical antipodes, (h) dextrorotatory, (i) Nicol prism, (j) superposable molecules, (k) meso isomer, (l) racemate, (m) racemization.

2. Write the structural formula for a compound which exhibits geometric as well as optical isomerism, and of a compound which has two asymmetric carbon atoms but is optically inactive.

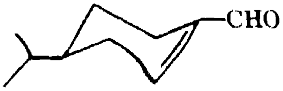
3. *From the following facts, determine a possible structural formula of A, $C_4H_8O_2$,* structures for the new compounds formed by addition of HCN to lactic aldehyde. How many different acids would result upon hydrolysis of the cyanohydrins produced? Are any of the acids meso isomers?

4. Which of the pentyl alcohols are optically active? Point out the asymmetric carbon atom in each of the optically active isomers.

5. Which of the following are optically active compounds: *n*-butanol; 4-hydroxyheptane; α-chlorobutyric acid; 1,2-dichloropropene; 1,2-epoxypropane?

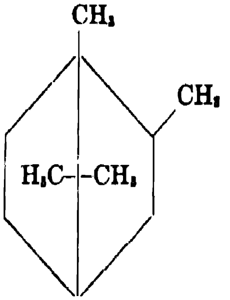
6. Cleavage of optically active methyl *sec*-butyl ether by anhydrous HBr gives primarily methyl bromide plus *sec*-butyl alcohol. The alcohol has the same configuration and essentially the same optical purity as the starting ether. (a) Offer an explanation for these results. Optically active *sec*-butyl alcohol is stable in aqueous alkali but racemizes in dilute sulfuric acid. (b) How do you interpret this behavior of *sec*-butyl alcohol?

7. Dihydrophellandric acid, when synthesized by oxidation of phellandral with ammoniacal silver nitrate and hydrogenation of the resulting acid, is a mixture of two optically inactive isomers. Give their structures and explain why each is optically inactive.



Phellandral

8. Draw structural formulas for all the stereoisomers possible for the formula



TEST QUESTIONS, Set 18

1. How many stereoisomers are possible with the formula $CH_3—CH═CH—CH(CH_3)—COOH$?

2. How could one separate and isolate the components in a mixture of *dl*-ethylpropylisobutylamine oxide, dihexylamine, *n*-octylamine, and *dl*-α-bromostearic acid?

3. From the following facts, determine a possible structure formula of A, $C_4H_8O_2$, and show how you reached your conclusion.

- (a) A reacts with 2,4-dinitrophenylhydrazine to yield a red precipitate, and A gives a red coloration with aq. ceric ammonium nitrate.
- (b) A reacts with acetyl chloride to produce a compound of molecular formula $C_6H_{10}O_3$.
- (c) A can be oxidized to a monocarboxylic acid B without the loss of carbon atoms.

(d) B is optically active and loses water when heated alone to give an unsaturated acid.

4. An optically active compound A, $C_7H_{14}O_2$, is hydrolyzed to give two compounds B, $C_5H_{10}O_2$, and C, C_2H_6O. B is optically active, water insoluble, but alkali soluble. C is water soluble. What is the structural formula of A, and how did you reach this conclusion?

5. How could one demonstrate that crotonic and isocrotonic acids are geometric isomers having the formula, $CH_3—CH=CH—COOH$?

6. An unknown substance, $C_7H_{15}NO$, hydrolyzes to give an amine and an acid. The amine reacts with nitrous acid to give a yellow-green, water-insoluble liquid. The acid is optically active. What is the structural formula of the unknown compound?

7. From the following facts, give the structural formula of the unknown compound A.

(a) A is an optically active compound, molecular formula $C_5H_{11}O_2N$.
(b) Upon hydrolysis of A, an optically active acid, $C_3H_6O_3$, and an amine are isolated.
(c) The amine reacts with benzenesulfonyl chloride to give an alkali-insoluble amide.

8. An optically active compound A, $C_3H_5O_2Cl$, dissolves in dilute alkali and is recovered unchanged upon acidification. What is its structural formula?

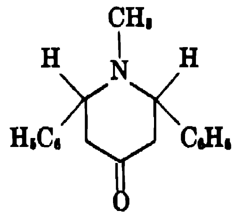
9. How many active and inactive isomers and racemic mixtures are there for the following formulas?

(a) $HOOC—(CHOH)_5—COOH$ (c) $OCH—(CHOH)_4—CH_2OH$
(b) $O=CH—(CHCl)_6—CHO$

10. Why is it that the physical properties of geometric isomers differ while those of optical isomers are the same?

11. A ketone having five carbon atoms yields an oxime whose reduction produces an amine with one asymmetric carbon atom. Write the structural formulas for possible original ketones, and for one whose structure is ruled out by the conditions imposed.

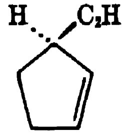
12. Should compound I be optically active?



I

Would you predict its oxime to be optically active?

13. Give the R-S nomenclature for



14. Give the structural formulas for 1(R),4(S)-methyl-2-norbornene and for the 1(S),4(R) isomer.

15. Should 1(S),2(R)-cyclohexanediol be optically active?

18

Organic Compounds of Sulfur and Phosphorus

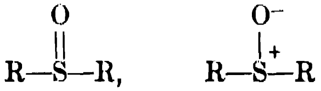
Organic compounds of sulfur and phosphorus are becoming increasingly important, but time in the first-year course does not permit more than a cursory treatment of these compounds.

18.1 TYPES OF SULFUR COMPOUNDS

Sulfur appears right below oxygen in the periodic table and is expected, therefore, to be dicovalent. In fact, sulfur forms many compounds analogous to those of oxygen in which sulfur occurs in place of oxygen.

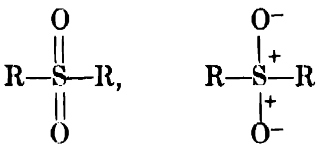
Oxygen Compound			*Sulfur Analog*
Alcohol	ROH	RSH	Mercaptan or alkanethiol
Ether	ROR	RSR	Sulfide or thioether
Peroxide	ROOR	RSSR	Disulfide
Acid	RCOOH	RCOSH	Thioacid
		RCSSH	Dithioacid
Aldehyde	RCHO	RCHS	Thioaldehyde or thial
Ketone	RCOR	RCSR	Thioketone or thione

By using *d* orbitals, sulfur and phosphorus may accommodate up to 18 electrons in their valence shells. Several types of compounds are known in which 10 or 12 electrons are in the sulfur or phosphorus valence shell. For such compounds, there is no single electronic structure. The molecules are resonance hybrids.



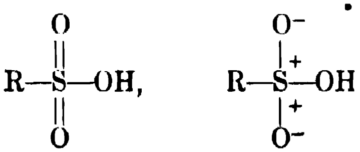
$$R-\overset{O}{\overset{\|}{S}}-R, \qquad R-\overset{O^-}{\overset{|+}{S}}-R$$

Sulfoxide



$$R-\underset{O}{\underset{\|}{\overset{O}{\overset{\|}{S}}}}-R, \qquad R-\underset{O^-}{\underset{|+}{\overset{O^-}{\overset{|+}{S}}}}-R$$

Sulfone



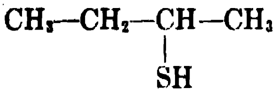
$$R-\underset{O}{\underset{\|}{\overset{O}{\overset{\|}{S}}}}-OH, \qquad R-\underset{O^-}{\underset{|+}{\overset{O^-}{\overset{|+}{S}}}}-OH$$

Sulfonic acid

In each of the compounds above, the organic groups may be aliphatic or aromatic.

18.2 MERCAPTANS

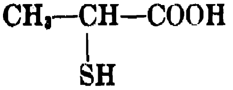
The I.U.C. system of naming mercaptans follows that for alcohols, with the suffix *-ol* changed to *-thiol.* When the alkyl group is a simple one, its name may be given, followed by the word *mercaptan.*



$$CH_3—CH_2—\underset{\underset{\displaystyle SH}{|}}{CH}—CH_3$$

2-butanethiol or *sec.*-butyl mercaptan

On the other hand, the —SH group may be regarded as a substituent, in which case it is called a *mercapto-*, *thiol-*, or *sulfhydryl* group. For illustration, $\underset{\underset{\displaystyle SH}{|}}{CH_3—CH}—COOH$ may be called α-mercaptopropionic acid.

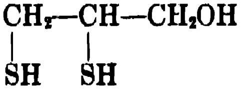


A common method of preparing mercaptans involves the replacement of halogens by the SH group (Sec. 9.4e).

$$R—X + KSH \rightarrow R—SH + KX$$

Mercaptans form much weaker hydrogen bonds than alcohols, owing to the electronegativity of sulfur being much lower than that of oxygen (cf. Sec. 10.5). As a result, mercaptans are lower boiling and less soluble in water than are alcohols. In sharp contrast to the bland odor of alcohols, mercaptans have extremely disagreeable odors. One of the constituents of the skunk secretion is *n*-butyl mercaptan. However, the offensive odor of mercaptans decreases with increasing molecular weight, and some of the heavy mercaptans have pleasant odors at high dilution. The lower mercaptans are very toxic, as is also hydrogen sulfide.

Mercaptans are weak acids and dissolve in aqueous alkali. They are readily precipitated by heavy metal ions. It is from such a reaction with mercury salts that the name mercaptan arose (L. *mercurium captans*, seizing mercury). During World War II, the British developed an antidote for the arsenical war gas Lewisite ($Cl—CH{=}CH—AsCl_2$). 1,2-Dithioglycerol or 2,3-dimercaptopropanol, called BAL for British Anti-Lewisite, blocks the toxic effect of arsenic compounds by forming stable reaction products with trivalent arsenic. This prevents the action of arsenic on enzymes containing thiol groups. BAL is now used as a general antidote for heavy metal poisoning.



$$\underset{\underset{\displaystyle SH}{|}}{CH_2}—\underset{\underset{\displaystyle SH}{|}}{CH}—CH_2OH$$

BAL

Mercaptans are easily oxidized. Mild oxidizing agents, such as iodine or air, convert thiols to disulfides.

$$2R{-}SH + I_2 \rightarrow R{-}S{-}S{-}R + 2HI$$

Stronger oxidizing agents, such as nitric acid or permanganate, carry the oxidation to sulfoxides, sulfones, or sulfonic acids. Sulfonic acids, like carboxylic acids, are stabilized by resonance and resist further action of oxidizing agents. Sulfides can be smoothly oxidized to sulfoxides with sodium periodate.

$$R_2S \xrightarrow{NaIO_4} R_2S{=}O$$

18.3 ARYLSULFONIC ACIDS

a. Preparation. Arylsulfonic acids are commonly prepared by sulfonation with concentrated sulfuric acid.[1]

$$\phi{-}H + HOSO_3H \rightarrow \phi{-}SO_3H + HOH$$

The SO_3H group is *m*-orienting and ring-deactivating, making it increasingly more difficult for di- and trisubstitution. This is unimportant, because one SO_3H group will usually serve most purposes.

The benzenesulfonic acids are strong acids, very soluble in water, and sparingly soluble in ether. This makes them somewhat difficult to isolate from the sulfonation reaction mixture. The mixture can hardly be evaporated because sulfuric acid boils at a high temperature. One procedure is to add carefully just the right amount of barium chloride solution to precipitate the sulfuric acid as $BaSO_4$, then boil off the water and HCl. This is tedious and exacting, because excess $BaCl_2$ would just add a new contaminant. The general practice is to precipitate the sodium or potassium salt by adding a large volume of saturated aqueous sodium or potassium chloride. The alkali salt precipitates as white crystals. Fortunately, the alkali salts may be used for most reactions and uses of arysulfonic acids.

b. Chemical properties.

Replacement by H:

$$\phi{-}SO_3H + HOH \xrightarrow[\Delta]{H_3O^+} \phi{-}H + HOSO_3H$$

This is the reverse of sulfonation. In strong, dilute acid, the SO_3H group is hydrolyzed off and the desulfonated product may often be steam distilled from the reaction mixture. The arylsulfonic acid is not steam distillable, since it is water soluble.

Replacement by OH:

$$\phi{-}SO_3Na + 2NaOH \xrightarrow{250^\circ} \phi{-}ONa + Na_2SO_3 + HOH$$

$$\xrightarrow{H_3O^+} \phi{-}OH$$

---

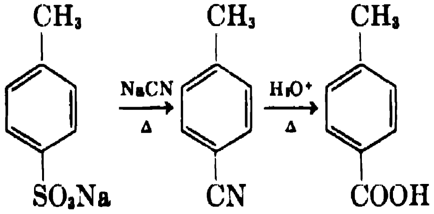
[1] An alternative method is to use SO_3 in liquid sulfur dioxide. The arylsulfonic acids are easily recovered from this reaction mixture.

The pyrolysis of the dry salts is carried out at the fusion point of NaOH. It provides one of the older methods of producing phenol commercially but is not used often in the laboratory. The common laboratory method of preparing phenols was taken up in Section 10.3c.

Replacement by CN:

$$\phi\text{—SO}_3\text{Na} + \text{NaCN} \xrightarrow{250°} \phi\text{—CN} + \text{Na}_2\text{SO}_3$$

Either the sodium or potassium salts may be used in these fusion reactions. This reaction is used for the preparation of benzonitriles only occasionally, since they may be prepared by more efficient reactions shown in Section 16.2d. This reaction may be used to verify the position of the SO_3Na group. The resulting cyanide is hydrolyzed to the acid, and the melting point of the acid compared with that of a known sample. For illustration:



p-Toluic acid

If the melting point of the product is identical to that of an authentic sample of *p*-toluic acid, then the SO_3Na group had to be *para* to the CH_3 group. In any other position, a different toluic acid isomer would result.

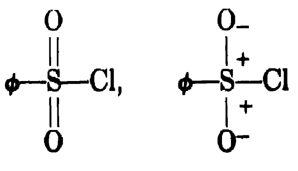
Benzenesulfonyl chlorides:

$$\phi\text{—SO}_3\text{Na} + \text{PCl}_5 \rightarrow \phi\text{—SO}_2\text{Cl} + \text{NaCl} + \text{POCl}_3$$

or

$$\phi\text{—H} + \text{HOSO}_2\text{Cl} \rightarrow \phi\text{—SO}_3\text{H} + \text{HCl}$$
$$\xrightarrow{\text{HOSO}_2\text{Cl}} \phi\text{—SO}_2\text{Cl} + \text{HOSO}_3\text{H}$$

Benzenesulfonyl chlorides may be prepared from a sodium benzenesulfonate and phosphorus pentachloride, or by reacting two moles of chlorosulfonic acid with a benzene derivative. The bond structure of the sulfonyl group is a resonance hybrid of two structures, with the larger contribution from the first form.

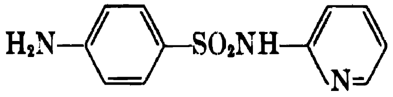


$$\phi\text{—}\overset{\overset{\text{O}}{\|}}{\underset{\underset{\text{O}}{\|}}{\text{S}}}\text{—Cl}, \qquad \phi\text{—}\overset{\overset{\text{O}^-}{|}}{\underset{\underset{\text{O}^-}{|}}{\text{S}^{++}}}\text{—Cl}$$

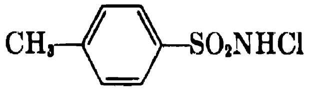
The benzenesulfonyl chlorides have chemical properties similar to those of carboxylic acid chlorides, the most prominent property being their reaction with compounds having active hydrogen atoms.

$$\phi\text{—SO}_2\text{Cl} + \text{HNR}_2 \rightarrow \phi\text{—SO}_2\text{NR}_2 + \text{HCl}$$

This reaction is used in the Hinsberg method of separating amines (page 412), which should be reviewed at this time. The product is an amide; therefore, it is easily recrystallized and is sharp melting. For this reason, they serve as good derivatives for confirming the identity of the corresponding benzenesulfonic acids or of primary and secondary amines. The reaction also offers a method of preparing many sulfa drugs.

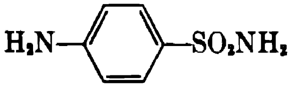


Sulfapyridine

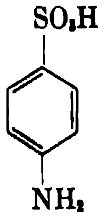


Chloramine T

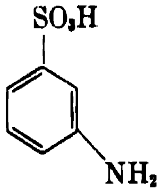
Sulfanilamide may be regarded as the parent of the sulfa drugs. Its name is derived from that of the corresponding acid.



Sulfanilamide



Sulfanilic acid

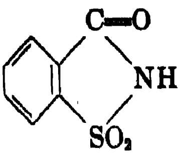


m-Aminobenzenesulfonic acid

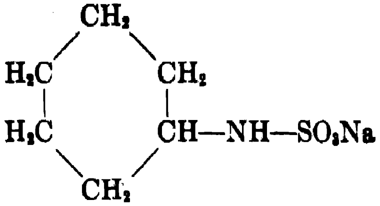
The *o*- and *m*-amino derivatives of benzenesulfonic acid are named as such, but the *para* isomer has the common name, sulfanilic acid.

18.4 USES OF SOME SULFUR COMPOUNDS

Derivatives of sulfonic acids have several uses. Mention has already been made of the Hinsberg separation of amines and of the miraculous sulfa drugs. Since the SO_3H group imparts water solubility, many dyes and drugs are sulfonated just to make them soluble in aqueous media. Saccharin and Sucaryl, the only two sweetening agents permitted by the Food and Drug Administration, are sulfur-containing compounds.



Saccharin
(306 times as sweet
as table sugar)

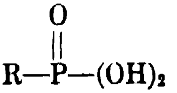


Sucaryl
(33 times as sweet
as table sugar)

The well-known agent of chemical warfare during World War I, *mustard gas*, is β-chloroethyl sulfide, $Cl—CH_2CH_2—S—CH_2CH_2—Cl$. It is a heavy, oily, liquid of boiling point 217° C. It was not used during World War II, perhaps as a result of the enemy's fear of retaliation.

18.5 PHOSPHORUS COMPOUNDS

Some of the more common organic phosphorus compounds are the phosphines, the phosphorous acids, and their esters:



$$R—\overset{\overset{\displaystyle O}{\|}}{P}—(OH)_2$$

Phosphonic acids

$R—P—(OR)_2$
Phosphonates

RPH_2
R_2PH
R_3P
Phosphines

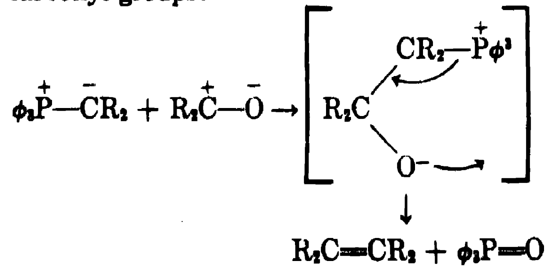
$(RO)_3P$
Alkyl phosphites

$(RO)_3P{=}O$
Alkyl phosphates

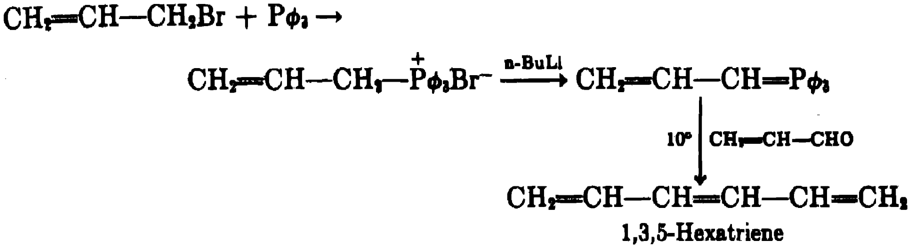
A highly useful class of phosphorus compounds for organic synthesis is that of the phosphorus ylenes, $R_3P{=}CR_2$. These are resonance hybrids of a polar and a nonpolar structure

$$R_3P{=}CR_2 \quad , \quad R_3\overset{+}{P}—\overset{-}{C}R_2$$

and the nucleophilic character of the carbon is shown by their reaction with alkyl halides or carbonyl groups:



Thus, this reaction, known as the *Wittig reaction*, provides a simple method of converting a $>$C=O group into a $>$C=CR$_2$ group. For example, compare this single step method to the sequence of reactions you used in response to question 21 in Test Question Set 12. A good illustration of the Wittig reaction is its use to prepare polyenes from simple starting compounds:



$$CH_2{=}CH{-}CH_2Br + P\phi_3 \rightarrow$$

$$CH_2{=}CH{-}CH_2{-}\overset{+}{P}\phi_3Br^- \xrightarrow{n\text{-BuLi}} CH_2{=}CH{-}CH{=}P\phi_3 \xrightarrow[10^\circ]{CH_2=CH-CHO} CH_2{=}CH{-}CH{=}CH{-}CH{=}CH_2$$

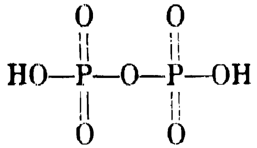
1,3,5-Hexatriene

By the same sequence of reactions, one could use cinnamaldehyde and 1,3-dibromopropane to prepare 1,9-diphenyl-1,3,6,8-nonatetraene:

$$BrCH_2CH_2CH_2Br + 2\phi CH{=}CH{-}CHO \rightsquigarrow$$

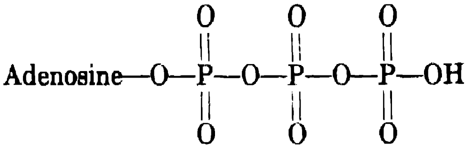
$$\phi{-}CH{=}CH{-}CH{=}CH{-}CH_2{-}CH{=}CH{-}CH{=}CH{-}\phi$$

Alkyl phosphates are used commercially as alkylating agents, and as high-temperature lubricants. Phosphoric acid anhydrides are extremely important in biological systems.



$$HO{-}\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{P}}{-}O{-}\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{P}}{-}OH$$

Pyrophosphoric acid



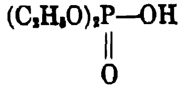
$$\text{Adenosine}{-}O{-}\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{P}}{-}O{-}\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{P}}{-}O{-}\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{P}}{-}OH$$

Adenosine triphosphate
(ATP)

When the anhydride bond is broken by hydrolysis, a large amount of energy is liberated. ATP is formed by the action of inorganic phosphate on the biological constituent adenosine (a complex nitrogenous sugar derivative), catalyzed by enzymes. When ATP reacts with other cell substances, considerable energy is released. Such a reaction provides the energy for many processes of organisms, such as muscle contraction, protein formation, fat degradation, and so forth.

STUDY EXERCISES

1. Give the name of sulfur analogues of the various classes of oxygen-containing organic compounds.
2. What is BAL, and what is its use?
3. Give names for the following compounds:

(a) $(CH_3)_2CH{-}SO_3H$
(b) $CH_3CH_2CHSHCH_2CH_3$
(c) $(C_2H_5O)_3PO$
(d) $CH_3{-}S{-}CH_2CH_2CH_3$
(e) $CH_3{-}SO_2{-}CH_2CH_2CH_3$
(f) 

$$(C_2H_5O)_2\underset{\underset{O}{\|}}{P}{-}OH$$

(g) $C_2H_5{-}SO{-}CH(CH_3)_2$
(h) $(CH_3O)_2POH$

4. Starting with alcohols or hydrocarbons, how can the following be prepared: (a) isopropyl mercaptan, (b) diethyl sulfide, (c) diethyl sulfate, (d) ethyl phosphate, (e) *p*-toluenesulfonamide, (f) *n*-propylsulfonic acid?

5. How could butyl mercaptan be separated from the fats found in the secretion of the skunk?

6. How could glycerol be separated from dithioglycerol?

7. Predict the better solvent for sulfoxides, chloroform or carbon tetrachloride, and explain the basis for your prediction.

8. How could one separate and isolate the components in the following mixtures without using fractional distillation other than the separation from ether: (a) toluenesulfonic acid, *p*-methylbenzoic acid, and toluene; (b) cyclohexylamine, benzoic acid, *p*-chlorotoluene, and N-methylcyclohexylamine?

19

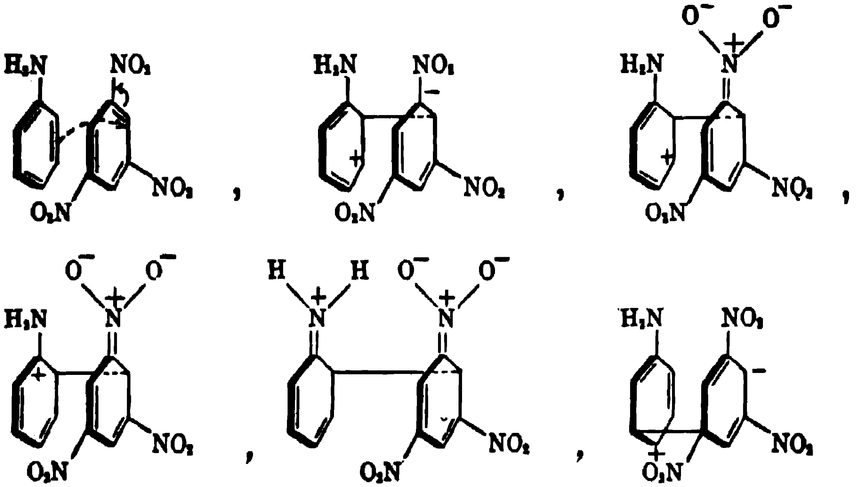
Molecular Association and Organometallic Compounds

19.1 CHARGE-TRANSFER COMPLEXES

In several places in this book, mention has been made of molecular addition compounds, such as the picrates of amines, and quinhydrone. No attempt was made to give the structures of these compounds, because the bonding between components is not easily symbolized as are covalent or simple ionic bonds.

For many years it has been known that certain substances combine in a 1:1 molar ratio to form crystalline addition products, referred to as *molecular addition compounds*. One component is always an electrophilic substance, i.e., electron seeking, and the other component is an electron-donor compound. X-ray diffraction studies have shown that the crystals of molecular addition compounds consist of alternate layers of the two components. What has puzzled chemists is the nature of the bonding between components. The bonding is not ionic, for solutions of the complexes are nonconducting. On the other hand, there is no typical covalent bond between an atom of one component and an atom of the other component. The major argument against this possibility is that the layers are too far apart for strong interatomic covalent bonding. Several theories have been advanced to account for this bonding. The most widely accepted view at this time is that there is a complex bond of partial ionic and partial covalent character between the two components. There is a loose electronic intermolecular interaction between components which gives rise to what has been called a charge-transfer bond or an *intermolecular coordinate covalent bond;* i.e., the bond has a covalent and an ionic character like a coordinate covalent bond in $H_3\overset{+}{N}—\overset{-}{B}X_3$. However, the covalent bonding is not between any two specific atoms, but between two molecules as a whole. One molecule, which can be designated A, is the electron-pair donor; and the other molecule, which shall be called B, is an electron-pair acceptor. The stability of the molecular addition compound is increased by having electron donating groups in A, and electron withdrawing groups in B. Accordingly, polynitro compounds (picric acid, trinitrobenzene, tetranitromethane, etc.) and quinones are the most common types used for the electron accepting component.

This concept of the bonding in molecular addition compounds cannot be symbolized by a single structural formula. In terms of resonance theory, the structure may be described as a resonance hybrid of forms such as the following, where aniline-trinitrobenzene is taken as an example. Keep in mind that the planes of the molecules are parallel, but not necessarily exactly face-to-face.



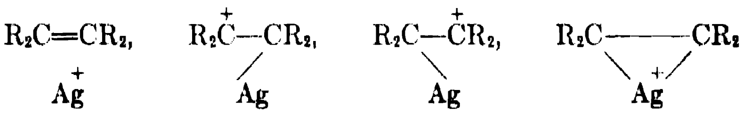
Many forms may be written in which the positive charge may reside on any of the carbons or the NH_2 group of aniline and the negative charge may reside on any of the carbons or NO_2 group of trinitrobenzene, and the bond between rings may involve any two carbons of each ring. Thus, the bonding between molecules does not involve any two specific atoms, and for this reason is called an *intermolecular bond*. There is an over-all sharing of an electron pair, giving the bond a covalent character, and still there is some ionic attraction between the fractional positive charge that arises on A and the fractional negative charge that arises on B. It can be seen, then, that the bonding is well described by the term *intermolecular coordinate covalent bond* and that it is too complex to be represented by conventional structural formulas.

Molecular addition compounds serve in a useful capacity in several ways. They are used for the isolation, purification, and identification of amines and polynuclear hydrocarbons. Most amines form picrates, for example, which serve as derivatives for the identification of the amines. The picrates may be formed, purified by recrystallization, and then decomposed in alkali to release the amine. In this fashion, an amine may be isolated from a reaction mixture in the form of its picrate, and subsequently recovered from the picrate. In recent years, much use has been made of silver nitrate complexes of alkenes for isolation of, and derivative formation from, the alkenes. In some instances, one can resolve *cis* and *trans* mixtures as a result of preferential complex formation of silver nitrate with one or the other isomer.

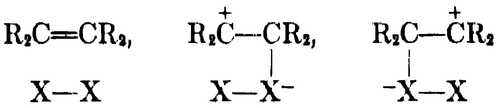
In addition to association through hydrogen bonds as discussed in Section 10.5, it has been observed in recent years that many substances associate in solution through charge-transfer bonds. For example, the electron-donor compounds, listed in Table 19.1, form molecular complexes with the electrophilic substances listed. These molecular complexes usually contain the components in a 1:1 molar ratio and are generally more deeply colored than their components. For instance, quinhydrones are composed of white hydroquinones and yellow quinones and are almost black.

The intercomponent bonding in the charge-transfer complexes is essentially the same in solution as in the solid state.

Again, the structures may be described as resonance hybrids of many forms, such as, for example, the structure of a silver ion-alkene complex:



and the structure of an alkene-halogen complex:



$$\begin{array}{c}R_2C{=}CR_2,\\ X{-}X\end{array}\qquad \begin{array}{c}R_2\overset{+}{C}{-}CR_2,\\ |\\ X{-}X^-\end{array}\qquad \begin{array}{c}R_2C{-}\overset{+}{C}R_2\\ |\\ {}^-X{-}X\end{array}$$

TABLE 19.1.

Electrophilic reagent + electron donor compound $\rightleftharpoons$ molecular complex

A		B	$\rightleftharpoons$ A:B, $^-$A—B$^+$
Halogens	+	Alkyl halides	
Picric acid		Alkenes	
Quinone		Aromatic hydrocarbons, amines, phenols, etc	
Ions of Ag, Cu, etc.		Alkynes	
Tetranitromethane			
Trinitrobenzene			

Charge-transfer complexes may play important roles in biological systems. For example, the substance in our eyes required for night vision, popularly called *visual purple*, consists of a pale-yellow organic compound bound to a colorless protein. The two components occur in a 1:1 molar ratio, giving the intensely colored, light-sensitive visual purple.

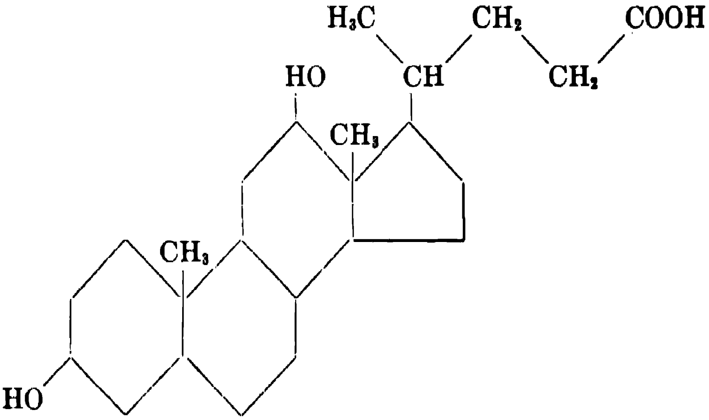
19.2 INCLUSION COMPLEXES

One of the most recently discovered complexes arising through molecular association are the *inclusion complexes*. They are crystalline compounds which arise when certain substances crystallize and entrap other molecules in the open cavities of the crystal lattices. For example, in the presence of straight-chain aliphatic compounds, urea crystallizes in the form of coils and entraps the straight-chain compounds down the center channels. Clean, crystalline complexes result.

There are three general types of inclusion complexes which differ in the shape of the hollow cavities of the crystal lattice network. One type has a channel-shaped cavity as mentioned above for the urea complexes. The starch-iodine complexes also are of this type. The polysaccharin chain forms a coil and traps the iodine molecules within the central channel. Amylose will include other types of molecules besides iodine—fatty acids, for example—and in the presence of fatty acids amylose does not give the blue color with iodine. Apparently the starch forms the colorless complex with the fatty acid in preference to the blue iodine complex. It is beyond the scope of this discussion to explain the blue color of the starch-iodine complexes. A second type of inclusion compound called *Clathrates* is a cage type in which the cavities have various polygonal shapes. This type is formed when, for example, hydroquinone or catechol crystals enclose small molecules like sulfur dioxide, formic acid, methanol, nitric oxide, oxygen, or the inert elements. The third type of inclusion compound is a layer type in which one substance crystallizes in layers and traps the foreign molecules between planes. Usually, the imprisoned molecules of inclusion compounds can be liberated by any process that destroys the crystal framework, such as melting or solvent action. There is no apparent chemical attraction between the components of these complexes. The binding forces are of the order of adsorption forces, i.e., van der Waals and dipolar forces.

The diameter of the tubular space of the urea complexes is fixed and only molecules with the dimensions to fit the channels will form complexes. It so happens that hydrocarbon straight chains fit snugly, but branched chains are too large. On the other hand, thiourea forms the same type of complex as urea, but the channel of the helix is larger in diameter. It is too large to hold straight-chain compounds, except the very long chains, but it will retain branched-chain and cyclic derivatives. Consequently, inclusion compounds provide a powerful tool for resolving mixtures, because their formation depends upon molecular shape and size. For example, it is known that branched-chain hydrocarbons make better motor fuels than straight-chain hydrocarbons, and removal of the latter through their urea complexes raises the octane rating of some petroleum products. One has only to mix the fuel with a saturated aqueous urea solution, and, after allowing time for the urea complex of the straight-chain hydrocarbons to precipitate, one can run off the upgraded fuel. In other instances, fats and waxes are purified by removing fatty acids in the form of their urea complexes. Substances may be stored in the form of their urea complexes for protection. Thus, autooxidizable materials, such as unsaturated oils and fatty acids, are completely stable when stored in the form of their urea complexes. Experiments are being done to use inclusion compounds for dispensing unstable food nutrients, such as vitamin A. Also, complexes of some optically active isomers have different solubilities, and some racemic mixtures have been resolved through their inclusion complexes.

It has been known for some time that the steroid desoxycholic acid forms layer-type inclusion compounds with many organic compounds, including hydrocarbons. These complexes, called *choleic acids*, dissolve in alkaline media



Desoxycholic acid

without decomposition; thus, they offer a means of getting hydrocarbons into aqueous solution. Such complexes appear to have an important function in biological systems. One theory for the assimilation of fats in the intestines is that steroidal compounds form soluble inclusion complexes with fats or hydrolyzed fats that diffuse across the cell membranes, and then release the fats or fatty acids after reaching the blood or lymph stream. In this connection, it is already known that aqueous solutions of sodium desoxyribonucleate and other purines (complex heterocyclic nitrogenous compounds) dissolve many aromatic amines and polynuclear hydrocarbons.

19.3 ORGANOMETALLIC COMPOUNDS

a. Simple-bonded compounds. Use has been made of organometallic compounds several times throughout the text. For instance, Grignard reagents and alkoxides have been used frequently. Organometallic compounds in which the metal is bonded to carbon may be largely ionic or largely covalent. Most alkali and alkaline earth organometallics consist of ions or ion pairs:

$\overset{-}{R}\overset{+}{Na}$	$\overset{-}{R}\overset{+}{Mg}X$	$\overset{-}{\phi}\overset{+}{Li}$	$R{-}C{\equiv}\overset{-}{C}\overset{+}{Na}$
Alkylsodium	Alkylmagnesium halide (Grignard reagent)	Phenyllithium	Sodium alkynide

$$\overset{-}{R}\overset{+2}{Zn}\overset{-}{R}$$

Dialkylzinc

Lithium compounds are exceptional in that they are fairly covalent and dissolve in hydrocarbon solvents. Some organometallic compounds of group IV elements and of transition metals are covalent:

R_4Sn	R_4Si	$R{-}C{\equiv}C{-}Ag$	$\phi{-}HgCl$
Tetraalkyltin	Tetraalkylsilane	Silver alkynide	Phenylmercuric chloride

Most organometallics involving metal-oxygen bonds are ionic (primarily because of the large difference in electronegativity between the metal and oxygen):

$NaOR$	ϕOK
Sodium alkoxide	Potassium phenoxide

Some organometallics are prepared from the respective alkyl or aryl halides in hydrocarbon or ether solvents:

$$n\text{-}C_4H_9I + Zn \rightarrow n\text{-}C_4H_9ZnI$$

$$C_6H_5Br + 2Li \rightarrow C_6H_5Li + LiBr$$

Some hydrocarbons are sufficiently acidic to react with metals directly:

$$R{-}C{\equiv}C{-}H + Na \xrightarrow{100^\circ} R{-}C{\equiv}CNa + \tfrac{1}{2}H_2$$

$$\phi_2CH_2 + K \xrightarrow{230^\circ} \phi_2CHK + \tfrac{1}{2}H_2$$

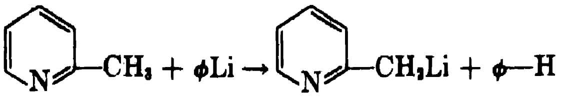
A few hydrocarbons will even react with sodium amide:

$$R{-}C{\equiv}C{-}H + NaNH_2 \rightarrow R{-}C{\equiv}CNa + NH_3$$

If an organometallic compound is mixed with a compound more acidic than the compound from which the organometallic is derived, an acid-base exchange will occur. For example, benzene reacts with an alkylsodium to give the alkane and phenylsodium:

$$\phi{-}H + RNa \rightarrow \phi Na + R{-}H$$

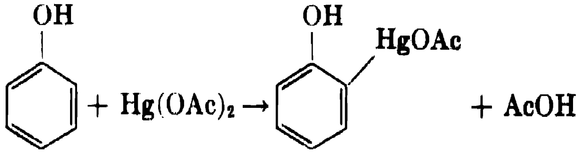
α-Picoline will displace benzene:



In this manner, the order of relative acidity of some hydrocarbons is found to be

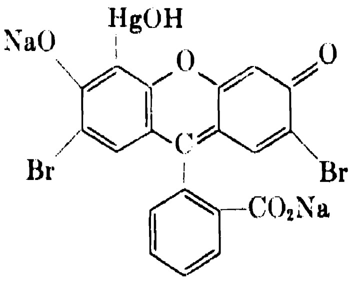
Alkane < benzene < toluene < triphenylmethane

Most of the arylmercurials are prepared by direct mercuration with mercuric acetate.

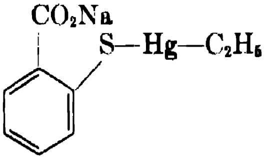


Much of the chemistry of the organometallics was discussed when the various compounds were used throughout this book. The major difference between the ionic and covalent compounds is that the ionic organometallics rapidly hydrolyze in water, whereas the covalent compounds are inert and insoluble in water. Most of the alkali and alkaline earth organometallics are rapidly oxidized in air. Some are even flammable in air.

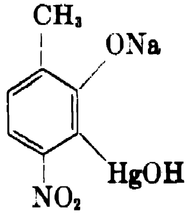
Several aromatic mercury compounds are used as antiseptics. An old one is *Mercurochrome*. Two which are much more potent are *Metaphen* and *Merthiolate*. These last two are colorless compounds, to which a red dye is added to increase public acceptance.



Mercurochrome



Merthiolate



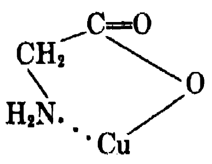
Metaphen

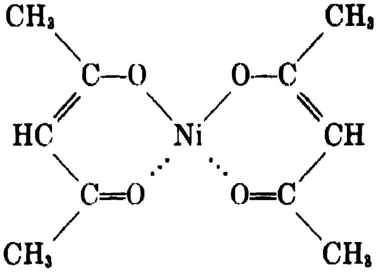
The most important lead compound is tetraethyllead. It is made from ethyl chloride and sodium-lead alloy.

$$4C_2H_5Cl + Na_4Pb \rightarrow (C_2H_5)_4Pb + 4NaCl$$

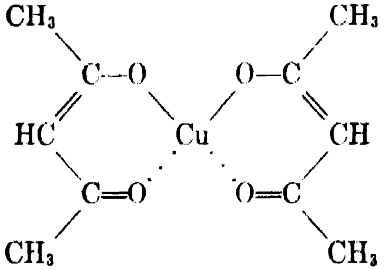
It is covalent like the mercury compounds; hence, it is stable in water, but may be cleaved in hydrochloric acid.

b. Chelates. The chelates constitute a very important class of organometallic compounds. When a molecule contains two coordinating atoms in such a position that they may form a ring with a third atom or ion, the resulting complex is called a *chelate compound*. The term *chelate* (pronounced *key-late*) is derived from the Greek word *chela*, meaning claw. The ring-closing atom is held in a molecular claw. Bond angle requirements restrict the most stable chelates to a five-membered, singly bonded ring, or a six-membered ring with two double bonds. The complexes of cuprous ion with glycine and of nickel ion with acetylacetone are examples of these two groups of chelates.

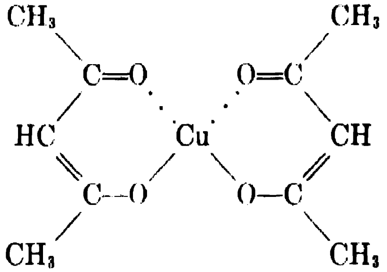




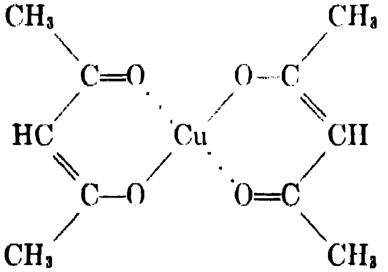
The dotted line is used to indicate the coordinate covalent bond, although in some chelates the two bonds to the central atom are identical or nearly so. For example, the four structures I–IV for cupric acetylacetone are equivalent, making the four bonds to copper identical; i.e., cupric acetylacetone is a



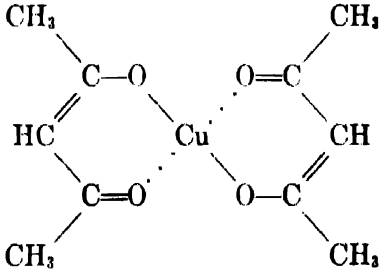
I



II



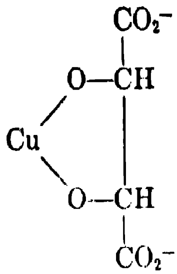
III



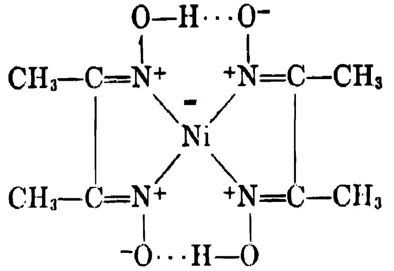
IV

resonance hybrid of I–IV. Amino nitrogen, and carbonyl, hydroxyl, and ether oxygen atoms possess unshared electron pairs, and are the most common atoms to form chelate rings with a metal ion.

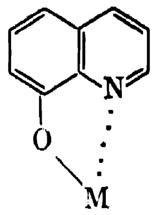
Chelates possess varying degrees of stability, water solubility, and ionic character. Those which are quite covalent are volatile and soluble in organic liquids. Chelates are used now in almost every field of chemical activity, ranging from dyestuffs through a broad application in analytical chemistry, to utilization in biological systems. Most applications make use of chelating organic compounds either to dissolve or to precipitate some metal ion. For instance, Fehling's solution uses tartrate ion to solubilize cupric ion in a basic solution, whereas dimethylglyoxime is used to precipitate nickel in analytical chemistry. In this connection, two compounds used extensively in recent years are 8-hydroxyquinoline (Oxine) and ethylenediaminetetraacetic acid (EDTA). *Versene* is a trade name of the tetrasodium salt of EDTA.



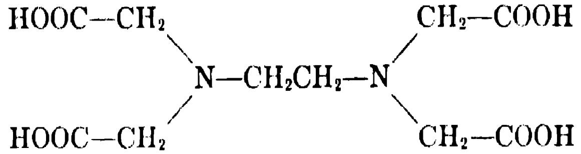
Cupric tartrate (ion of Fehling's solution)



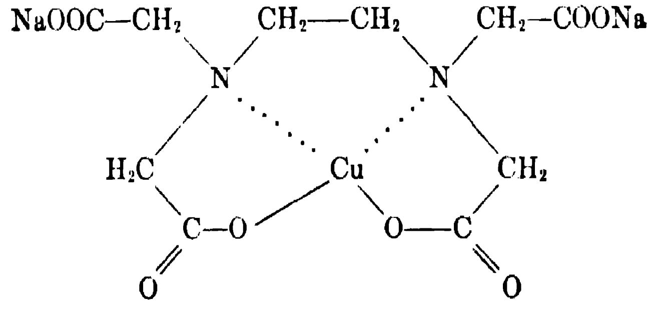
Nickel dimethylglyoxime



Univalent metal chelate of Oxine



EDTA

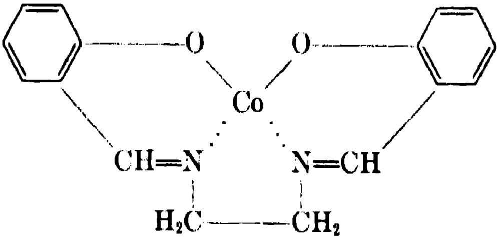


Copper ethylenediaminetetraacetate

EDTA is usually used to hold metal ions in solution, and Oxine is used to precipitate ions. The solubility of chelates may be altered by changing the *p*H of the medium, and considerable specificity may be achieved by proper manipulation of conditions. For illustration, the selective precipitation of ions in a mixture of tungsten, iron, and aluminum may be done as follows. At *p*H = 5, Oxine precipitates all three ions quantitatively, but in the presence of EDTA, only tungsten is precipitated; i.e., iron and aluminum form soluble chelates with EDTA which are too stable at this *p*H to be precipitated by Oxine. However, the iron-oxine chelate may be precipitated by raising the *p*H to 8–9. This leaves the aluminum in solution, which may be precipitated at a still higher pH. Many such selective precipitations or dissolutions of metals have been developed for a wide variety of applications, as can be seen from the following partial list of uses of chelates:

Dyeing or bleaching textiles
Antioxidants
Ion exchange separations
Water softeners
Qualitative and quantitative analysis
Supplying nutrients and mineral deficiencies to agricultural crops
Stabilization of pharmaceuticals
Radioactivity decontamination
Production of rubber, metal finishes, leather, and miscellaneous commodities
Removal of metal poisons from living systems

An interesting use of chelates not listed above is the reversible adsorption of gases. Salcomine is capable of selectively adsorbing oxygen from cold air (resembling hemoglobin in this capacity) and of evolving the pure gas when heated to 50° to 60°. As a result, a chamber of Salcomine can serve as a supply of pure oxygen and is safer to use than a cylinder of liquid oxygen.



Salcomine

c. Molecular sandwich compounds. The methylene hydrocarbons of cyclopentadiene are sufficiently acidic to react with alkali metals and Grignard reagents. The cyclopentadienyl ion, $C_5H_5^-$, may be attached to a metal in one of three ways:

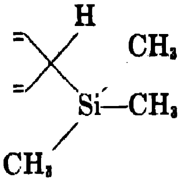
1. By an ionic bond, as is the case with alkali metals and in Grignard reagents.

$$C_5H_6 + Na \rightarrow C_5H_5Na + \tfrac{1}{2}H_2$$

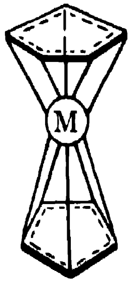
$$C_5H_6 + RMgX \rightarrow C_5H_5MgX + RH$$

These organometallics are crystalline salts, hydrolyze in water to liberate cyclopentadiene, are insoluble in hydrocarbons but fairly soluble in ethers, and usually react slowly with air.

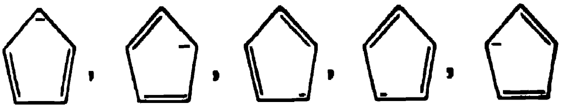
2. By an *interatomic covalent* bond as in $C_5H_5Si(CH_3)_3$.



3. By an *intermolecular coordinate covalent* bond. This third type of compound is formed primarily with the transition metals Fe, Co, Ni, Cr, etc., which have available *d* orbitals. Crystalline samples have been analyzed by X-ray diffraction and found to consist of the metal "sandwiched" between two parallel cyclopentadienyl rings. The first compound of this type to be discovered and the most extensively studied is *bis*-(cyclopentadienyl)-iron, $(C_5H_5)_2Fe$, commonly called *ferrocene*. Ferrocene is an orange, crystalline solid, which melts at 173° to 174° and boils near 249°. It is readily soluble in common organic solvents, such as benzene, ether, and alcohol. In these sandwich compounds, each cyclopentadienyl ring exhibits aromatic character (cf. Section 7.7). For example, these compounds do not undergo a Diels-Alder reaction with maleic anhydride (cyclopentadiene does), they are not hydrogenated over platinum catalyst, they undergo substitution reactions like the Friedel-Crafts reaction, side chains may be oxidized without affecting the rings, and they do not polymerize. To account for the covalent character of the complexes (verified by magnetic susceptibility measurements) and the aromatic character of the cyclopentadienyl rings, these sandwich compounds have been given a pentagonal antiprismatic structure as in I, where M is initially a metal cation. Infrared absorption spectra reveal that all carbon-carbon bonds are identical, and dipole moments suggest that the rings may rotate freely. In the complex, each cyclopentadienyl ring is a resonance hybrid of five completely equivalent structures.



I



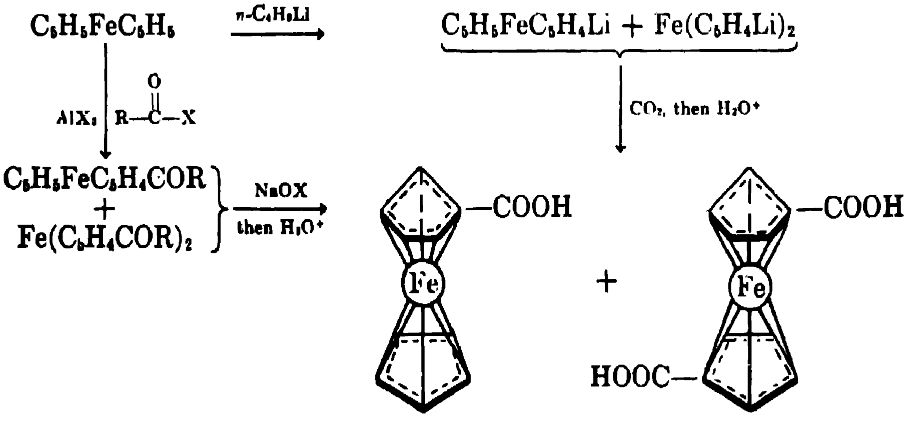
Thus, the metal is equally bonded to each carbon atom, and the bonding is well described by the term *intermolecular coordinate covalent bond*. It represents exactly what is meant by covalent bonding, because each component, the metal ion and a cyclopentadienyl ring, behaves as if it has the extra electron pair although neither has it completely. The metal is not ionic; hence it acts as if it has accepted the electron pair, and at the same time, each cyclopentadienyl ring can be aromatic only if it has the electron pair. Consequently, the electron pairs are shared and each participant is as stable as if the electron pair belonged solely to it.

The molecular sandwich compounds, as well as the molecular addition compounds, reveal the ability of aromatic rings to share electrons in a direction perpendicular to the plane of the rings. Other aromatic rings, including benzene, have been found to form these sandwich compounds.

The sandwich compounds can be easily prepared from cyclopentadienylsodium.

$$2C_5H_5Na + MCl_2 \rightarrow (C_5H_5)_2M + 2NaCl$$

They are typical aromatic compounds. Ferrocene, for example, is insoluble and unaffected by H_2O, alkali, and even boiling concentrated hydrochloric acid. Ferrocene can be metalated or acetylated and then converted to the *mono*- and *bis*-(carboxyl)-ferrocenes.



*Mono*carboxylferrocene *Bis*-(carboxyl)-ferrocene

Most oxidizing agents oxidize the iron to the ferric state to produce "ferricinium ion." Aqueous solutions of the ion are red when concentrated and blue when dilute. Because of oxidation of the iron, ferrocene cannot be halogenated or nitrated.

Ferrocene is used commercially for promoting smokeless combustion of fuels. Other potential uses are to serve as antiknock agents, antioxidants, paint driers, and as catalysts for various organic reactions.

STUDY EXERCISES

1. Describe the bonding in (a) amine picrates, (b) ferrocene, (c) Grignard reagents, (d) cuprous alanine, $CH_3CHNH_2CO_2Cu$.

2. What is (a) a molecular addition compound, (b) a molecular sandwich compound, (c) a chelate, (d) a charge-transfer bond, (e) an inclusion complex, (f) a use of picrates, (g) a use of inclusion compounds of urea.

3. How do inclusion compounds of urea and desoxycholic acid differ?

4. What possible role might inclusion complexes play in digestion?

5. Name and give the structures of two organometallic compounds having extensive commercial or domestic use.

6. How would one prepare (a) *n*-propylzinc iodide, (b) tetramethyllead, (c) 2-hydroxy-3-methyl-phenylmercuric acetate?

7. Which would be the more ionic, a Si—O or a C—O bond?

8. Explain the fact that benzene is less soluble in aqueous KNO_3 than in water, but more soluble in aqueous $AgNO_3$ than in water.

9. How can an impurity of *n*-decane be removed from a sample of Isooctane gasoline?

10. What facts point to the aromatic character of the cyclopentadienyl rings of ferrocene?

11. What are two uses of chelates? Try to explain how the chelate might function in each of the two uses and compare your description with those given in a reference book or by your instructor.

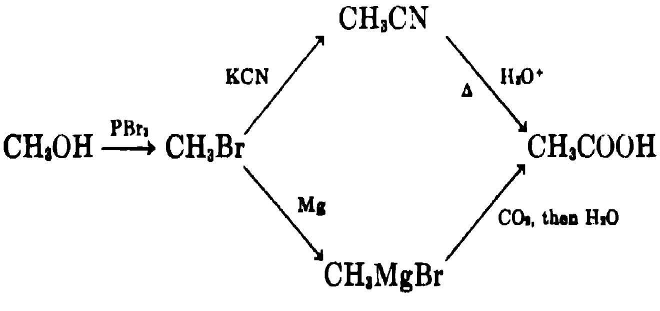
12. Lithium acetylacetonate is sparingly soluble in chloroform and has a very high melting point, whereas beryllium acetylacetonate is soluble in chloroform and boils at 270° (m.p. 108°). What do you infer from these properties about the nature of the metal-organic bonding in these compounds?

20

Suggestions for a Review

In the foregoing chapters we have discussed the chemistry of the common functional groups. Future chapters will be concerned with more complex substances containing many functional groups, but little additional basic organic chemistry will be encountered. It is appropriate, therefore, to review the organic chemistry learned up to this point in order to get it well organized. We have discussed many chemical reactions, and some form of systemization is needed to coordinate most of this information.

It is probably apparent by now that there is a substantial list of organic type-reactions that form the foundation of organic chemistry. In order to do any synthesis or analysis of organic compounds, these general type-reactions must be known, for although some may be deduced on a basis of reaction mechanisms, they still must be known from memory in order to plan syntheses or analyses *with dispatch*. For example, to work out a synthesis of acetic acid from methyl alcohol, a chemist would use reactions such as



and these must be familiar enough that he can think of them promptly. He would soon be dismissed as a chemist if he had to figure out these reactions by reaction mechanisms or analogy each time he wanted to use them. Of course, he may have to do this in planning new reactions or for unusual syntheses. It is the same for writing structures of organic compounds. At first, the student must concentrate in order to picture or draw the structures of isobutane, propylene, acetic acid, etc., and must check back to see if valence rules have been observed. Without special efforts to memorize these structures, he is soon able to write them almost subconsciously merely from usage and frequent contact. For complex compounds, he must apply the principles of nomenclature to arrive at the structure, but if he had to do this also for the most common compounds, he would be regarded as a poor organic chemist.

As previously stated, there is a basic group of organic reactions that must be known in order to do any work in organic chemistry expeditiously, and this is the group which the beginning organic student must learn. This does not mean rote memorization, however. Through use and association, these reactions become familiar without conscious effort to memorize them. It is specifically for this purpose that the Study Exercises should be worked. Then, to test one's progress and development, the Test Questions should be solved.

One type of exercise is to give general equations for the preparation of each class of compound studied, i.e., preparation of alcohols, aldehydes, amines, etc. A second form of exercise is to state the reagents and conditions for transforming a given class of compound directly into another given class, that is, to indicate, for example, how an alkyl halide would be changed into a nitroalkane, or how a carboxylic acid would be reduced to an alcohol. A third sort of exercise is to use these reactions for the qualitative identification of a given class or for the qualitative distinction between two or more classes. For example, a chemist distinguishes an unsaturated hydrocarbon from a saturated hydrocarbon on the basis of the difference in their reactions with bromine or aqueous permanganate. A fourth kind of exercise, and the one which requires the greatest recollection of the type-reactions, is to figure out a sequence of reactions for multistep syntheses: for example, to work out the preparation of *n*-butyl alcohol from *n*-propyl alcohol or the preparation of adipic acid from phenol. Each one of these forms of exercise has been practiced all along in the Study Exercises and Test Questions.

It is also apparent that many of the general reactions were encountered several times for different purposes. Thus, the reaction of $RCOOH + R'OH \rightleftarrows RCOOR' + HOH$ was considered among the chemical properties of alcohols, then among the chemical properties of acids, then as a preparative method for esters, and finally as a chemical property of esters. To help the student recognize the interrelationships among the most common type-reactions, the following exercises and summaries are given. These should prevent him from getting the impression that organic chemistry is just a mass of unrelated reactions.

20.1 RECOMMENDED PLAN FOR REVIEW

For the reasons stated in the Foreword and in Section 2.3, the student is urged to study with a small group. The following plan is recommended for students planning to make a comprehensive review. The essential points suggested have been incorporated into the Study Exercises and Test Questions, so that the student who has been doing well all along should start his review at step 5 below and make certain that he can answer virtually all the Test Questions up to this point in the book. Students who have been away from organic chemistry for an interval of time, and those doing poorly in the current course should review as follows:

1. Write down the general equations for the preparation and chemical properties of each class of compound taken up in class.

2. On a separate sheet, make up a list of questions asking for a reproduction of these general equations; for example, "give three general equations for the preparation of primary alcohols." Then write examples of each of these equations using real substances, i.e., not just general equations in which R groups are used, but with specific structural formulas. Questions of the type described here are usually the first few among the Study Exercises.

3. Familiarize yourself with the physical properties of each class of compound taken up, attention being given to water solubility, ether or sulfuric acid solubility, acid or base character, and whether associated or not. Such properties form the basis for carrying out *separations* of different classes of compounds. Questions of this type are included in the Test Questions.

4. Note the differences in chemical properties of each class of compound taken up which permit their qualitative test-tube differentiation. Questions of this type are included in the Test Questions.

Note: When stating how to distinguish one compound from another, indicate what one would observe in order to know that a certain process has taken place. For example, in distinguishing valeraldehyde from ethyl ketone, do not say, "use Tollens' reagent, only the valeraldehyde will react." Rather, say, "the valeraldehyde will reduce Tollens' reagent, producing a silver mirror or black precipitate, whereas the ketone will not." Thus, one always uses a method which will produce a visible change, such as a precipitate, a color, a gas, an odor, a solution, etc.

5. Give the reagents and conditions for crossing each of the arrows in the chart in Figure 20.1. The arrows are numbered so that answers corresponding to the numbers may be written on a separate sheet of paper.

6. Given any one of the following classes of compounds, write the series of laboratory reactions that could be used to prepare any of the other classes: alkane, alkene, alkyne, alkyl halide, alcohol, aldehyde, oxime, nitrile, amide, ester, carboxylic acid, acid chloride, amine, and nitroalkane. Specify catalysts when such are normally used.

Give the series of reactions that could be used in the laboratory to replace any one of the following groups when attached to a benzene ring by any one of the others: $—NO_2$, $—NH_2$, $N{=}N—\phi$, $—CH_3$, $—CH_2OH$, —CHO, —COOH, COOR, $—SO_3H$, —H, —CN, $—\phi$, $—CH_2X$, —X. For instance, start with nitrobenzene to prepare benzoic acid, bromobenzene, or toluene; or start with chlorobenzene to prepare nitrobenzene, benzoic acid, phenol, or azobenzene.

7. Practice using the malonic ester and acetoacetic ester syntheses for

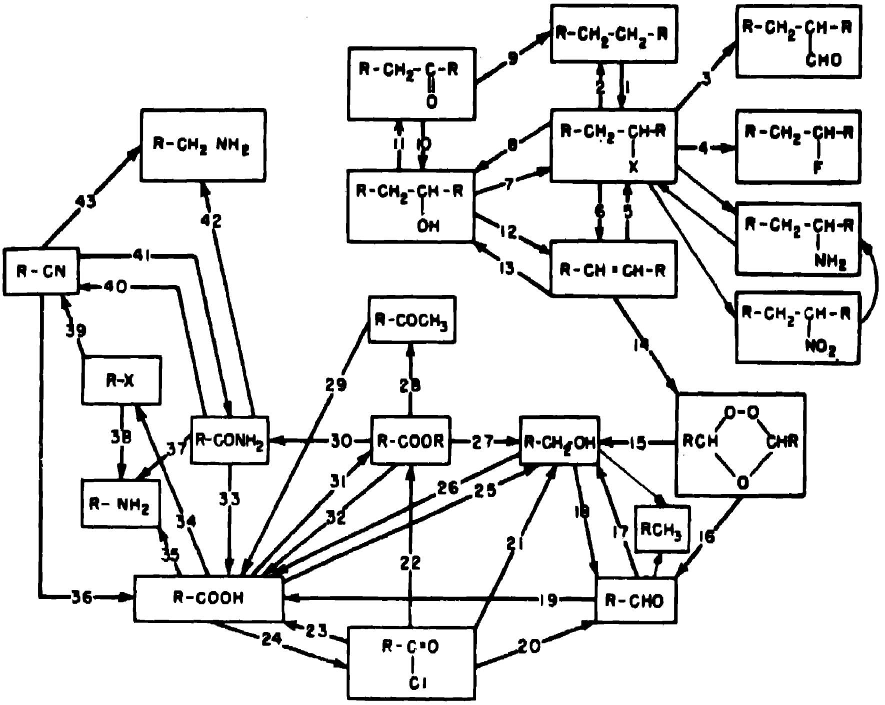


Fig. 20.1. Interreaction chart for the aliphatic compounds.

preparing substituted acetic acids, and using the acetoacetic ester synthesis also for preparing methyl ketones. Write out the series of consecutive reactions for multistep syntheses to go from a given compound to the next higher or next lower homolog, i.e., ROH to RCH_2OH, or RCH_2NH_2 to RNH_2.

An occasional task of an organic chemist is to prepare the next higher, or next lower homolog of a given class of compounds. For this purpose, common methods for increasing or decreasing a carbon chain by one carbon atom are summarized below. These reactions have already been discussed throughout the text. Many reactions are chain-lengthening reactions, such as the Wurtz reaction and the aldol condensation, but these reactions add several carbon atoms and frequently the problem is to increase the chain by only one carbon atom.

DEGRADATION METHODS

$$\text{RCOOH} \xrightarrow[\Delta]{\text{NaOH, CaO}} \text{R—H (for electronegative R groups)} \qquad (1)$$

$$\left.\begin{matrix}\text{RCOOH}\\ \text{RCOCl}\\ \text{RCOOR}'\end{matrix}\right\} \xrightarrow{\text{HN}_3} \text{R—NH}_2 \qquad (2)$$

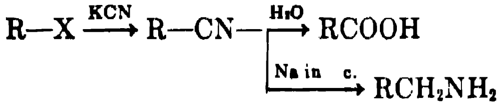
$$\text{RCONH}_2 \xrightarrow[\Delta]{\text{Br}_2\text{, NaOH}} \text{R—NH}_2 \qquad (3)$$

$$RCOOAg \xrightarrow[\Delta]{X_2,\ CCl_4} R{-}X \qquad (4)$$

$$R{-}COCl \xrightarrow[\Delta]{Ag_2O,\ X_2} R{-}X \qquad (5)$$

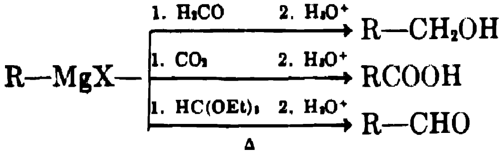
$$RCOCH_3 \xrightarrow[\Delta]{X_2,\ NaOH} RCOONa \qquad (6)$$

CHAIN-LENGTHENING METHODS



(7)

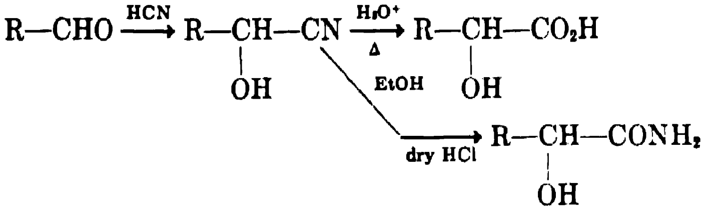
$$RC{\equiv}CH \xrightarrow{1.\ NaNH_2 \quad 2.\ CH_3I} RC{\equiv}C{-}CH_3 \qquad (8)$$



(9)

(10)

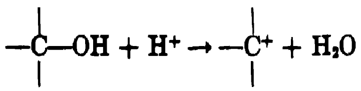
(11)



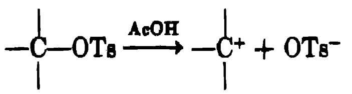
(12)

$$R{-}COCl \xrightarrow[2.\ Ag_2O,\ H_2O]{1.\ CH_2N_2} R{-}CH_2{-}COOH \qquad (13)$$

REACTIONS PRODUCING CARBONIUM IONS

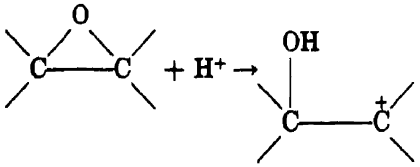


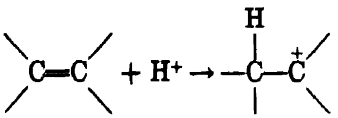
$$-\overset{|}{\underset{|}{C}}-OH + H^+ \rightarrow -\overset{|}{\underset{|}{C}}{}^+ + H_2O$$

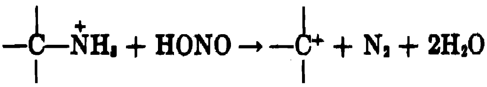


$$-\overset{|}{\underset{|}{C}}-OTs \xrightarrow{AcOH} -\overset{|}{\underset{|}{C}}{}^+ + OTs^-$$

Ts = tosylate

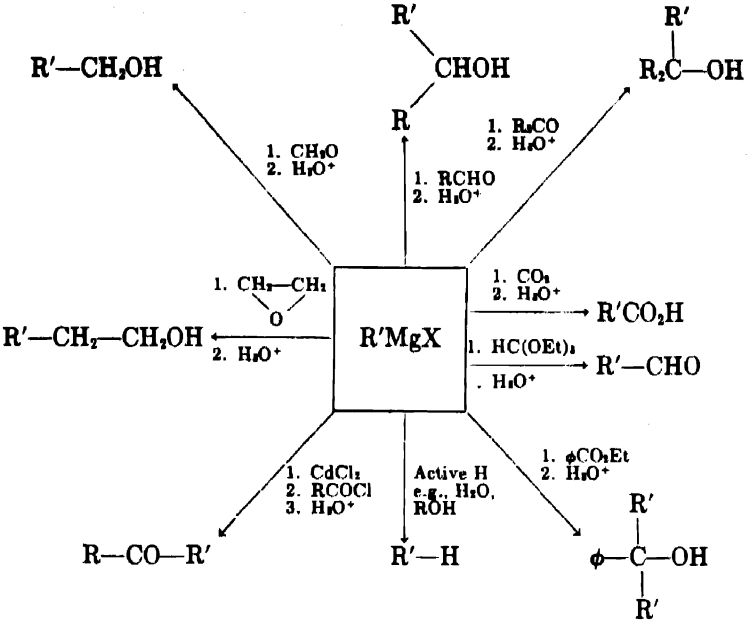






$$-\overset{|}{\underset{|}{C}}-\overset{+}{N}H_3 + HONO \rightarrow -\overset{|}{\underset{|}{C}}{}^+ + N_2 + 2H_2O$$

REACTION CHART FOR A GRIGNARD



8. Give the reagents and any special conditions which could be used in the laboratory to carry out the following:

i. Dehydrations

1. $\phi_2C(OH)—CH\phi_2 \rightarrow \phi_2C═C\phi_2$
2. $\phi—CH═NOH \rightarrow \phi—C≡N$
3. $\phi—CONH_2 \rightarrow \phi—C≡N$

ii. Hydrolyses

1. $\phi—CCl_3 \rightarrow \phi—COOH$
2. $\phi—CH(OAc)_2 \rightarrow \phi—CHO$
3. $\phi_2C(OR)_2 \rightarrow \phi_2CO$
4. $\phi—CH═NOH \rightarrow \phi—CHO$
5. $\phi—MgX \rightarrow \phi—H$
6. $\phi—CHCl_2 \rightarrow \phi—CHO$
7. $\phi—C≡N \rightarrow \phi—CONH_2$
8. $\phi—CN \rightarrow \phi—CO_2H$
9. $\phi—CO—CH_2—CO_2C_2H_5$
   $\rightarrow \phi—CO—CH_3$
10. $CH_3—CO—C\phi_2—CO_2C_2H_5$
    $\rightarrow \phi_2CHCOOH$

9. State in one sentence each a contribution made to organic chemistry by the persons listed below. If it is for a reaction, an equation for the reaction will serve best.

1. Wurtz
2. Oppenauer
3. Williamson
4. Hunsdiecker
5. Meerwein, Ponndorf, and Verley
6. Fischer and Tropsch
7. Bergius
8. Markownikoff
9. Diels and Alder
10. Thiele
11. Hofmann
12. Cannizzaro
13. Hinsberg
14. Gabriel
15. Claisen
16. Arndt and Eistert
17. Schotten and Baumann
18. Schmidt
19. G. N. Lewis
20. H. C. Brown

21. Grignard
22. Tollens
23. Clemmensen
24. Kekulé
25. Von Baeyer
26. Perkin
27. Ullmann
28. Sandmeyer
29. Friedel and Crafts
30. Kolbe and Schmitt
31. A. Nobel
32. A. C. Cope or V. Prelog
33. Fittig
34. Strecker
35. Sommelet
36. Beckmann
37. Schiemann
38. Rosenmund
39. Gattermann
40. Reformatsky
41. Wolff and Kishner
42. Walden
43. Reimer and Tiemann
44. Lucas
45. Saytzeff
46. Michael
47. Pauling
48. Pasteur
49. Birch
50. Hückel

This type of question comprises some memory work but is a measure of maturity in organic chemistry, because organic chemists refer to many reactions, theories, and reagents by the names of their discoverers or contributors. For example, rather than give word equations for the reactions involved, a chemist would say that he used *n*-propyl bromide in a Wurtz reaction, or the Hofmann degradation of acetamide, or the Oppenauer oxidation of 2-hexene-4-ol. The student should be able to visualize these reactions promptly when they are referred to. The more names one knows which are associated with significant chemical contributions, the more chemical conversations or articles he will be able to understand. The same is true in other fields, such as medicine.

10. The specificity of organic redox reactions has been stressed throughout this book; for review, the student should indicate at least one reagent which can be used for carrying out the following oxidations or reductions in the laboratory. The answers may be found in the respective sections of the book.

Oxidations

1. $\phi\text{—CH}_2\text{OH} \rightarrow \phi\text{—CHO}$
2. $\phi_3\text{C—H} \rightarrow \phi_3\text{C—OH}$
3. $\phi\text{—CH}_3 \rightarrow \phi\text{—CHO}$
4. $\phi\text{—CH=CHCH}_2\text{OH} \rightarrow \phi\text{—CH=CHCHO}$
5. $\phi\text{—CH=CH—R} \rightarrow \phi\text{—CHO}$
6. $\phi\text{—NH}_2 \rightarrow \phi\text{—NO}_2$
7. $\phi\text{—CH=CH—}\phi \rightarrow \phi\text{—CHOH—CHOH—}\phi$
8. $\phi_2\text{C(OH)—C(OH)}\phi_2 \rightarrow 2\phi_2\text{CO}$
9. $\text{CH}_3\text{—C}_6\text{H}_{11} \rightarrow \text{CH}_3\text{—C}_6\text{H}_5$
10. $\phi\text{—CH}_2\text{Cl} \rightarrow \phi\text{—CHO}$
11. $\phi\text{—NH—NH—}\phi \rightarrow \phi\text{—N=N—}\phi$
12. $\phi\text{—NHOH} \rightarrow \phi\text{—NO}$
13. $\phi\text{—CH}_3 \rightarrow \phi\text{—COOH}$
14. $\text{R—SH} \rightarrow \text{R—S—S—R}$
15. Phenol → Quinone
16. $\text{R}_2\text{CHOH} \rightarrow \text{R}_2\text{CO}$
17. $\text{R—CHO} \rightarrow \text{R—COOH}$

Reductions

1. $\phi\text{—CHO} \rightarrow \phi\text{—CH}_2\text{OH}$
2. $\phi\text{—NO}_2 \rightarrow \phi\text{—NH}_3^+$
3. $\phi\text{N}_2^+ \rightarrow \phi\text{—H}$
4. $\phi\text{—NO}_2 \rightarrow \phi\text{—N=N—}\phi$
5. $\phi\text{—NO}_2 \rightarrow \phi\text{—NH—NH—}\phi$
6. $\phi\text{—NO}_2 \rightarrow \phi\text{—N}^+\text{(O}^-\text{)=N—}\phi$
7. $\phi\text{—NO}_2 \rightarrow \phi\text{—NHOH}$
8. $\phi\text{—COOR} \rightarrow \phi\text{—CH}_2\text{OH}$
9. $\phi\text{—CONH}_2 \rightarrow \phi\text{—CH}_2\text{NH}_2$
10. $\phi\text{—CH}_2\text{CH}_2\text{NO}_2 \rightarrow \phi\text{—CH}_2\text{CH}_2\text{NH}_2$
11. $\phi\text{—CH}_2\text{Cl} \rightarrow \phi\text{—CH}_3$
12. $\phi\text{—COCl} \rightarrow \phi\text{—CHO}$
13. $\phi\text{—CN} \rightarrow \phi\text{—CH}_2\text{NH}_2$
14. $\phi\text{—COCl} \rightarrow \phi\text{—CH}_2\text{OH}$
15. Quinone → Hydroquinone
16. $\text{R}_2\text{CO} \rightarrow \text{R}_2\text{CH}_2$
17. $\text{R}_2\text{CO} \rightarrow \text{R}_2\text{CHOH}$
18. $2\text{R}_2\text{CO} \rightarrow \text{R}_2\text{C(OH)—C(OH)R}_2$
19. 3-Hexene ozonide → $2\text{CH}_3\text{CH}_2\text{CHO}$

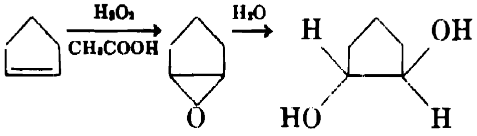
Oxidations

18. $R—COCH_3 \rightarrow R—COOH$
19. $R—CH_2CH_2COOH \rightarrow R—COOH$
20. $R—CO—CHOH—R$
    $\rightarrow R—CO—CO—R$

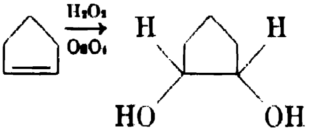
Reactions

20. 3-Hexene ozonide → $2CH_3CH_2CH_2OH$
21. $p\text{-}O_2N—C_6H_4—CH{=}CH—CHO \rightarrow$
    $p\text{-}O_2N—C_6H_4—CH{=}CH—CH_2OH$
22. Benzene → 1,4-cyclohexadiene

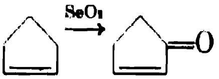
An example of the variation in products obtained with a variety of oxidizing agents is found in the oxidation of cyclopentene. If hydrogen peroxide in glacial acetic acid is used, the initial product is cyclopentene oxide, which can be hydrolyzed to *trans*-1,2-cyclopentanediol.



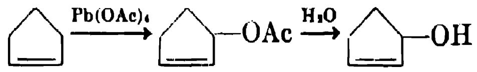
Oxidation of the olefin with hydrogen peroxide in the presence of osmium tetroxide yields *cis*-1,2-cyclopentanediol.



Oxidation with selenium dioxide will produce 2-cyclopentenone.



If lead tetraacetate is used, among the products is 3-acetoxycyclopentene, which can be hydrolyzed to 3-cyclopentenol.



The several oxidizing agents lead to different products because they react by different mechanisms.

11. Review the nomenclature, special uses, industrial preparation of each class of compound taken up, and the chemistry of rubber and petroleum.

For practice, name the substance or substances in list B which would be selected for uses found in list A:

A. Uses

1. Fungicide
2. Moth repellent
3. Antifungus agent on military equipment
4. Fumigant
5. Rodenticide
6. High explosive
7. Herbicide
8. Skin mosquito repellent

B. Substances

1. Methyl bromide
2. Pentachlorophenol
3. 1080
4. BAL
5. RDX
6. $n\text{-}C_{18}F_{38}$
7. Copper naphthenate
8. *p*-Dichlorobenzene
9. 2,4-D

A. Uses

9. Detergent
10. Heavy metal-poisoning antidote
11. Paint drier catalyst
12. Emulsifying agent for rubber vulcanization
13. Tobacco moistening agent
14. Radiator antifreezing agent
15. High-temperature lubricant
16. Nontoxic fire extinguisher
17. Anesthetic
18. Refrigerant
19. Water softener
20. Insecticide spreader

B. Substances

10. Morphine
11. Sodium dodecylbenzene sulfonate
12. Sucaryl
13. Manganese linoleate
14. Nylon
15. Reserpine
16. Diethyl toluamide
17. Silicone
18. Lucite
19. Melmac
20. Freon
21. EDTA
22. Celluloid
23. Bakelite
24. Polythene
25. Cyclopropane
26. Trifluoromethyl bromide
27. Teflon
28. Ethylene glycol
29. Aluminum stearate
30. Glycerol

12. Explain the various physicochemical principles and theories taken up, and *demonstrate* their application; i.e., cite experimental observations which justify the concept or principle:

Isomerism, tautomerism, steric hindrance, association, 1,4-addition, homology, resonance, Markownikoff's rule, induction, hydrogen bonding, etc.

A good student will have a clear distinction in his mind between: (a) hydrolysis, hydration, and hydrogenation, (b) oxidation and reduction, (c) tautomerism and resonance, and (d) isomerism, isomerization, and isomers.

13. Be able to make calculations connected with extraction, oxidation-reduction reactions, and quantities based on stoichiometry, such as gas laws, per cent yields, neutralization, esterification, hydrolyses, addition reactions, etc.

14. *See your instructor for assistance when needed.*

20.2 COMPLEX METAL-HYDRIDE REDUCTIONS

One very effective method of reviewing and consolidating one's knowledge of organic chemistry is to approach the subject from a different point of view. Since the subject matter in this book is divided into chapters on the basis of the major classes of compounds, a new approach is to consider a general reaction that applies to many of them. One such reaction is reduction by complex metal hydrides.

Complex metal hydrides are exemplified by the versatile reducing agents lithium aluminum hydride and sodium borohydride. Since the war, the selective reduction of various functional groups through the use of these metal hydrides has accomplished certain useful syntheses that heretofore were impractical, inconvenient, or impossible. For example, the laboratory reduction of carboxylic acids to alcohols was not done before the appearance of $LiAlH_4$.

Most of the metal hydrides react violently with water. In this case, an etheral solution of the metal hydride is used. If the substance to be reduced is insoluble in an ether solvent (dioxane, ethyl ether, or tetrahydrofuran) or in a hydrocarbon, it can be reduced by an extraction technique; that is, the substance is placed in the thimble of a Soxhlet extractor over a refluxing etheral solution of the metal hydride. Some metal hydrides, such as sodium borohydride, may be used in aqueous solutions and offer an advantage from this standpoint.

The lithium aluminum hydride reductions appearing in this book up to this point can be listed as follows:

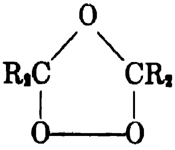
$$\left.\begin{array}{l} RCOOR' \\ RCOOH \\ RCOCl \\ RCHO \end{array}\right\} \xrightarrow{LiAlH_4} RCH_2OH$$

$$R_2C{=}O \xrightarrow{LiAlH_4} R_2CHOH$$

$$\left.\begin{array}{l} RCN \\ RCH_2NO_2 \\ RCONH_2 \end{array}\right\} \xrightarrow{LiAlH_4} RCH_2NH_2$$

$$RCONR_2 \xrightarrow{LiAlH_4} RCH_2NR_2$$

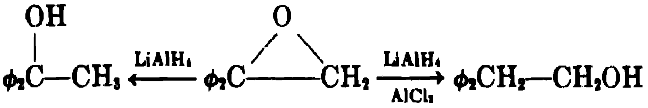
$$R{-}X \xrightarrow{LiAlH_4} R{-}H$$



$$\xrightarrow{LiAlH_4} 2R_2CHOH$$

$$2\phi NO_2 \xrightarrow{LiAlH_4} \phi{-}N{=}N{-}\phi$$

Many other metal hydrides have been studied, such as the aluminum hydrides of magnesium, sodium, and calcium, and the borohydrides of lithium, sodium, potassium, and calcium. Furthermore, many other types of reductions are possible, some of which are quite specific. For example, lithium gallium hydride reduces aliphatic, but not aromatic aldehydes, ketones, and nitriles; sodium borohydride reduces acid chlorides, but not carboxylic acids and anhydrides. $LiAlH_4$ reduces acid chlorides to the corresponding alcohols whereas lithium tri-*t*-butoxyaluminohydride [Li-(t-$BuO)_3AlH$] reduces acid chlorides to aldehydes. The selectivity of these reductions can be made even greater by combining the metal hydrides with Lewis acids such as aluminum chloride. For example, haloacids, R –CHX—COOH, can be reduced to the corresponding alcohols without loss of the halogen atom, and nitrocarbonyls may be reduced to the respective alcohols without reduction of the nitro group. Also, the spatial size of the metal hydride-$AlCl_3$ mixture can affect the course of certain reductions, this mixture favoring the least hindered product. For example,



Some of the common functional groups reducible with certain metal hydrides are tabulated in Table 20.1. The usual reduction products have

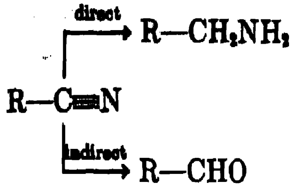
TABLE 20.1. SOME SELECTIVE METAL HYDRIDE REDUCTIONS AT 25–80°C.

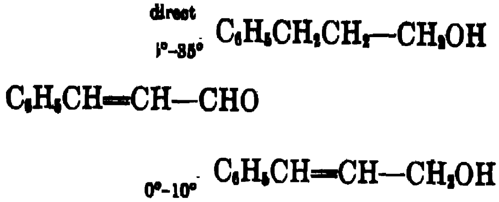
Class of Compound	$LiAlH_4$	$NaBH_4$	$NaBH_4$ + $AlCl_3$	$NaBH_4$ + $LiBr$	Pyridine-BH_3
Aldehydes	++	++	++	++	++
Ketones	++	++	++	++	++
Acid chlorides	++	++	++	++	++
Esters	++	– –	++	+	– –
Acids	++	– –	++	– –	+
Amides	++	– –			
Salts	++	– –	– –	– –	
Nitriles	++	– –	++	– –	
Nitro compounds	+	– –	– –	– –	

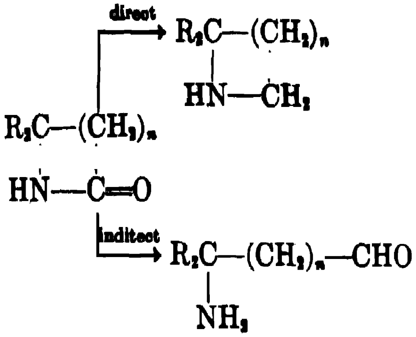
++ Reacts rapidly; + reacts at moderate rate; – – reacts very slowly or negligibly.

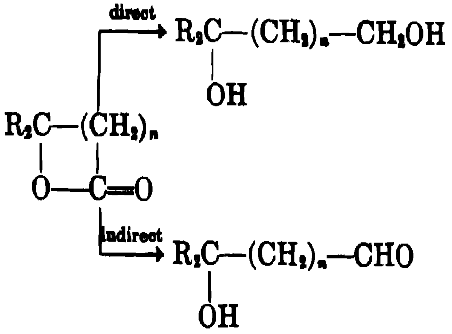
been given at the respective places in the text. It can be seen from the table, for example, that $NaBH_4 + AlCl_3$ will selectively reduce an ester group in the presence of a carboxylate salt, and pyridineborane will reduce an acid but not an ester group.

Furthermore, the course of an oxidation or reduction is influenced by the experimental conditions. For illustration, reductions with lithium aluminum hydride (LAH) are generally carried out by one of two methods: (i) The "direct" method consists of the addition of a solution of the compound to be reduced to a solution of LAH. (ii) The "inverse" method involves the addition of a LAH solution to the compound to be reduced. Often, the two procedures yield different products because, in the direct method, an excess of reducing agent is always present, making the reaction less specific than in the indirect method. Several examples are given on page 491.


direct
R—CH₂NH₂
R—C≡N
indirect
R—CHO


direct
5°-35°
C₆H₅CH₂CH₂—CH₂OH
C₆H₅CH═CH—CHO
0°-10°
C₆H₅CH═CH—CH₂OH


direct
R₂C—(CH₂)ₙ
HN—CH₂
R₂C—(CH₂)ₙ
HN—C═O
indirect
R₂C—(CH₂)ₙ—CHO
NH₂


direct
R₂C—(CH₂)ₙ—CH₂OH
OH
R₂C—(CH₂)ₙ
O—C═O
indirect
R₂C—(CH₂)ₙ—CHO
OH

21

Functional Group Analysis and Structure Determination

The method used for performing an analysis of an organic material naturally depends upon its complexity, its properties, and what is sought from the analysis. A frequent problem is the determination of the structural formula of a compound, commonly called *structure determination.* To do this, a chemist first isolates the compound, perhaps by an extraction. Then he purifies it by an appropriate technique, probably by fractional crystallization, fractional distillation, or one of the chromatographic fractionation procedures. He then measures certain characterizing properties such as melting point, boiling point, or solubility (in water, ether, dilute acid or base, or sulfuric acid). Next, he will probably make an analysis for the elements present, usually by the sodium fusion procedure. On the basis of which elements are present and the solubility properties, he will make chemical and physical qualitative tests for the functional groups present. Certain quantitative functional group analyses may be made too, such as titration of COOH groups to get an equivalent weight, or reaction with nitrous acid to determine the number of primary amino groups present, and so on.

From all this information the chemist should get an idea of possible structures for the compound. He then checks reference books and the literature for comparison with known compounds. If any known compounds have properties identical or almost identical with those observed for his unknown, he makes a derivative of his unknown and compares its melting point with that recorded in the literature for the possible known compound. Probably two different derivatives will be made for confirmation. If the compound has not been previously prepared and reported in the literature, the chemist will carry out a quantitative composition analysis for comparison with the calculated composition of a proposed structural formula. If the unknown is a complex one, it may have to be broken into simpler molecules, the fragments identified separately, and a structural formula for the original compound deduced on a basis of the structures of the fragments.

The fragments are put together like a jigsaw puzzle in order to construct a complete structure for the complex unknown. The assigned structure must then be confirmed by a synthesis of the substance. This general procedure can be summarized as follows:

1. Isolation, purification, observation of appearance, odor, color, etc.
2. Measurement of solubility characteristics and physical constants such as melting or boiling point, index of refraction, spectral properties, etc.
3. Fusion and analysis for elements present.
4. Chemical and physical functional group analysis.
5. Possible structure assignment by check with literature.
6. Confirmation through derivatives.

If no "fit" is found, then the following steps can be taken:

7. Composition analysis and molecular weight determination.
8. Additional chemical and physical functional group analysis and perhaps some quantitative analyses, i.e., determination of number of OH groups present, etc.
9. Degradation and similar analysis of fragments.
10. Deduction of structure.
11. Confirmation by synthesis.

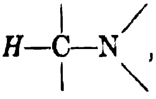
Some of these steps may often be omitted, depending upon the circumstances. For example, the source of the sample may make it possible to circumvent step 3, or spectra of the sample may provide conclusive evidence for the structure and make step 6 unnecessary. We have commonly accepted the belief that two compounds are identical if they have identical physical properties, i.e., melting point and index of refraction, etc. The more properties that are found to be the same, the stronger is our confidence that the samples are truly identical.

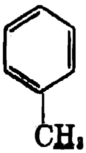
An absorption spectrum such as the infrared constitutes thousands of properties, since it shows the absorption of light at thousands of different frequencies. Identical spectra for two different samples, then, provides very conclusive evidence that the two samples are identical.

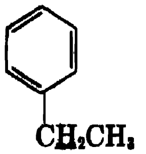
An important part of this identification procedure is step 4, namely, functional group analysis. Tests are developed on a basis of the *differences* in chemical properties of the various classes of compounds. Most of these tests have been used throughout this book for distinguishing one or two different classes of compounds, such as a primary from a secondary alcohol, or an aldehyde from a ketone. However, when a functional group analysis is made, the student will learn that seldom is a test unique for a single class of compound. For example, the liberation of hydrogen with sodium metal does not indicate an alcohol exclusively, because any compound with an active hydrogen atom will also liberate hydrogen gas, such as a 1-alkyne, amine, or an acid. Reduction of permanganate does not indicate solely an unsaturated hydrocarbon, because other compounds, such as phenols and anilines, are readily oxidized. For this reason, considerable thought must be used in interpreting the tests. The student must keep in mind which other classes of compounds might give positive results in any given test.

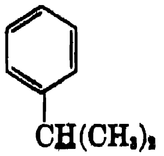
Qualitative classification tests are described below for some functional groups. An attempt has been made to arrange them in an order which will give the least interference from other groups. Thus, a test is made for a carbonyl compound first, because virtually none of the other classes of compounds will give a positive test with the reagent used. Hydrocarbons are the last group to be recognized, and this is done by elimination. Seldom does a person have to perform all the tests. For example, if the sodium fusion analysis reveals an absence of nitrogen in the compound, then the tests for amines and nitro groups need not be performed. Or, if the solubility properties show that the compound is not an acid, then the test for a phenol need not be made.

Phenomenal advances have been made in the chemist's ability to resolve mixtures and determine the structures of compounds, and the principal factor responsible for this marked progress has been the use of physical instruments such as the various types of spectrophotometers and chromatographic paraphernalia. Very often a structure can be assigned on the basis of physical measurements alone. A major advantage of the physical methods is that they need very small samples, and in many cases the samples could be recovered if desired. Also, the physical methods are usually very rapid and in some cases the results can be read directly from a chart during the analysis.

Some of these instrumental techniques are rapidly working their way into the classroom. In order to give the student some experience at least in making use of such data, some of the spectral characteristics of the common functional groups are given along with their chemical tests. These data are only probable ranges for each functional group, and for a more precise value one should look up the data for a model compound. For instance, the n.m.r. τ value for a proton on a carbon attached to nitrogen,  $H{-}\overset{|}{\underset{|}{C}}{-}N\langle$, will depend upon whether the carbon has two, one, or no other carbons attached, whether the N is acyclic or cyclic, and whether secondary or tertiary. Similarly, the τ value of a methyl proton is affected by substitution on the carbon. For example,







τ = 7.36 7.38 7.13

A brief discussion of the basic theory of the physical methods was given

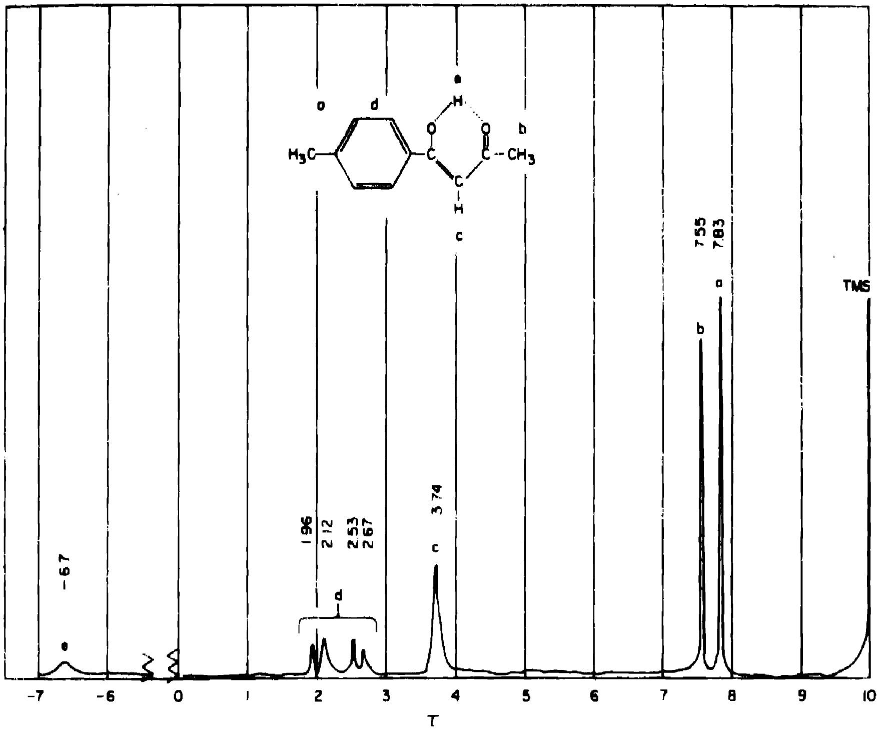


Fig. 21.1. Spectrum of $p\text{-}CH_3—C_6H_4—C(OH) = CH—CO—CH_3$ in CCl_4 at 60 mc. TMS = tetra methylsilane internal standard.

in Chapter 6, and additional comments on the relationships between molecular structure and spectra are given in Section 21.3. Illustrative spectra are drawn in Figures 3.3, 21.2 (infrared), 6.2 (ultraviolet), 6.3, and 21.1 (n.m.r.). Examine these spectra as the spectral characteristics of the respective groups are discussed in Section 21.1.

21.1 FUNCTIONAL GROUP CHEMICAL TESTS[1] AND SPECTRAL CHARACTERISTICS[2]

1. **Test for carbonyl compounds.** If a liquid, add 1–2 drops of the sample to 3–5 ml of 2,4-dinitrophenylhydrazine reagent. If a solid, dissolve 3 small crystals in 0.5 ml of ethanol or dioxane, and add 3–5 ml of the 2,4-dinitrophenylhydrazine reagent. The formation within 5 min of a yellow to red precipitate is a positive test. For comparison, try the test on butyraldehyde or benzaldehyde.

a. Aldehyde from ketone: In a thoroughly clean test tube, place 2 ml of Tollens' 1 reagent (dilute $AgNO_3$) and add Tollens' 2 reagent (ammoniacal, aqueous NaOH) drop

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[1] Most of the chemical tests in this section are derived from R. L. Shriner, R. C. Fuson, and D. Y. Curtin, *Systematic Identification of Organic Compounds*, 4th ed., 1956, John Wiley & Sons, Inc., and are used here with the permission of the authors and publisher.

[2] IR = infrared absorption data. UV = ultraviolet absorption data. n.m.r. = nuclear magnetic resonance proton peaks in τ values.

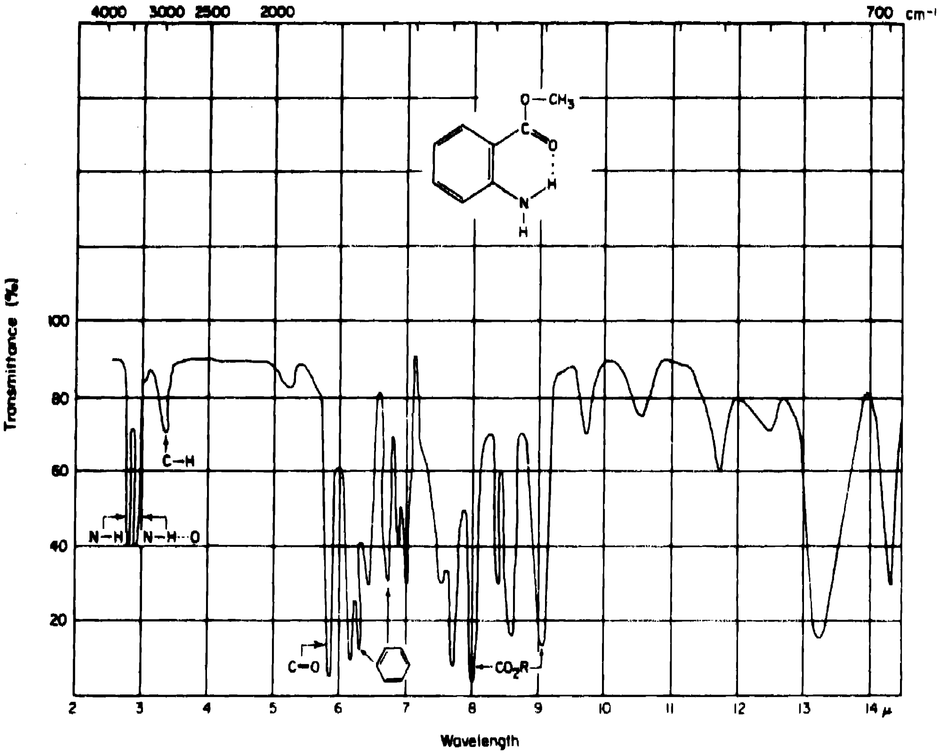

Fig. 21.2. Infrared absorption spectrum of methyl anthranilate.

by drop, with constant shaking, until the precipitate of silver oxide just dissolves. In order to obtain a sensitive reagent, it is necessary to avoid a large excess of ammonia. Add 3–4 drops or crystals of the unknown and shake vigorously. The formation of a black precipitate or silver mirror within 5 min is a positive test for an aldehyde (or α-hydroxy ketone). For comparison, try the test on butyraldehyde or benzaldehyde.

b. Aliphatic from aromatic aldehyde: To a solution of 0.2 g of the sample in water or dioxane, add 5 ml of Benedict's solution, and heat the mixture to boiling. A precipitate, colored orange or green (depending on the amount of sample used), is a positive test for an aliphatic aldehyde. For comparison, try the test with butyraldehyde *and* benzaldehyde.

SPECTRAL CHARACTERISTICS

	Infrared	*Ultraviolet*
Sat. C=O (footnote 3)	$\nu_{co} = 1720\text{–}1740\ \text{cm}^{-1}$	$\lambda_m = 185,\quad 280\ \text{m}\mu$ $\epsilon \geq 10^4 \quad < 50$
C=C—C=O and φ—C=O	$\nu_{co} = 1670\text{–}1690\ \text{cm}^{-1}$	$\lambda_m = 220\text{–}260,\quad 300\text{–}350\ \text{m}\mu$ $\epsilon = 10^4 \quad < 50$
C=O···H—O	$\nu_{co} = 1600\text{–}1640\ \text{cm}^{-1}$	

---

[3] The values for cyclic ketones vary widely with ring size.

n.m.r.

$X = -CHO$	$-\overset{O}{\overset{\Vert}{C}}-R$	$-\overset{O}{\overset{\Vert}{C}}-\phi$	$-COOH$
τ for $\underline{H}-C-X = 7.6\text{–}7.83$	7.52–7.9	7.38	7.43–7.93

τ for $COC\underline{H}_3 = 8.0\text{–}8.2$

2. Test for phenols.[4] Dissolve or suspend about 0.1 g of solid or 1 drop of liquid of the substance to be tested in 1 ml of methyl alcohol. Add 2 drops of the methanolic ferric chloride reagent and 1–3 drops of pyridine. Phenols and enols give a vivid color change. For comparison, try the test on an alkylphenol, a halophenol, or salicylaldehyde.

INFRARED SPECTRAL CHARACTERISTICS

Substance	*Monomolecular*		*Associated*		
	ν_{O-H}		$\nu_{O-H\cdots O}$		ν_{C-O}
Alcohols, 1°	3640 cm^{-1}		3350 cm^{-1}	(broad)	1050 cm^{-1}
2°	3630		3350	(broad)	1100
3°	3617		3350	(broad)	1150
Phenols	3643	(intermol.)	3608	(broad)	1200
		(intramol.)	~3100	(broad)	
Carboxylic acid	3520		3075		
Chelated enol			2600–2800	(broad)	

3. Test for acids. Dissolve a small portion of the sample in water or aq. alcohol, and find out if it is acid to litmus or methyl orange. If the sample is insoluble, attempt to dissolve a pinch or large drop in 5 ml of dilute NaOH. If the sample is thrown out of solution upon acidification with dilute H_2SO_4, the unknown is an acid. The acid may be a carboxylic acid, polynitroalkane, phenol, or any substance acidic enough to dissolve in dilute aq. alkali.

Infrared: See under phenols for ν_{O-H} and under acyl groups for $\nu_{C=O}$.

n.m.r.:

$$\tau \text{ for } \underline{H}-\underset{|}{\overset{|}{C}}-COOH = 7.43\text{–}7.93$$

4. Test for alcohols. *a.* For water-soluble compounds: Dilute 0.5 ml ceric nitrate reagent with a 3-ml portion of distilled water, add 4–5 drops of the compound to be tested, shake the mixture, and note the change in color. If the compound is a solid, dissolve it in water, and add 4–5 drops of water solution to the reagent.

For water-insoluble compounds: To 0.5 ml of the reagent, add 3 ml of dioxane. If a precipitate forms, add 3–4 drops of water with shaking until the solution is clear. Add 4–5 drops or crystals of the compound to be tested, shake, and note the color.

A positive test for an alcohol is indicated by a change in the color of the reagent from yellow to red. For comparison, try the test on *n*-butyl, *sec*-butyl, and *t*-butyl alcohols.

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[4] S. Soloway and S. H. Wilson, *Anal. Chem.* **24**, 979 (1952).

b. Primary from secondary from tertiary alcohols: To 1 ml of the alcohol in a test tube, add 10 ml of Lucas reagent at room temperature. Stopper the tube and shake the mixture; then allow the mixture to stand. Note the time required for the formation of a turbidity.

If there is difficulty in interpreting your results, use a second type of test as follows. Add 1 ml of the sample to 3 ml of glacial acetic acid, and add a saturated, filtered solution of $KMnO_4$ in water, drop by drop, with stoppering and vigorous shaking of the test tube. If no decolorization occurs, the alcohol sample is tertiary. If decolorization takes place, continue adding $KMnO_4$ solution until the pink color persists. Then add a drop of conc. H_2SO_4, and add more $KMnO_4$ solution. If the pink color is discharged, the sample is a secondary alcohol; if no decolorization occurs, the alcohol is primary. Run a blank test on glacial acetic acid to check for impurities in it.

Infrared: See under phenols.

n.m.r.:

	$C\underline{H}_3OH$	$RC\underline{H}_2OH$	$R_2C\underline{H}OH$
τ =	6.62	6.44	6.14

5. Test for acyl compounds. Heat together 1 part of the unknown, 1 part of hydroxylamine hydrochloride, 1 part of solid sodium hydroxide, and 5 parts of 80% alcohol for 10 min on the steam bath. Cool the mixture, and dilute it with 4 volumes of water, shake it, and carefully add dilute hydrochloric acid until it is very slightly acidic to litmus paper. Then add 2 drops of aq. $FeCl_3$. A violet or red color indicates the presence of a hydroxamic acid, which is formed from an ester, acid anhydride, acid halide, lactone, or carboxylic acid.

SPECTRAL CHARACTERISTICS

Infrared	ν_{C-O-C}	$\nu_{C=O}$
RCOOR	1160–1250 cm^{-1}	1735–1750 cm^{-1}
CH_3COOR	1236–1247	1735–1750
ϕCOOR	1100–1150 *and* 1250–1310	1717–1730
RCOOϕ		1776
RCOOH		1700–1725
RCOCl		1770–1815
Cyclic $(RCO)_2O$		1750–1800 *and* 1820–1870
6-Membered lactone		1735–1750
5-Membered lactone		1760–1780
	ν_{N-H}	$\nu_{C=O}$
$RCONH_2$	3450 (doublet)	1590–1615 *and* 1665
RCONHR	3450 (singlet)	1520 *and* 1665
$RCONR_2$	none	1665

n.m.r.	X =	$-CO_2R$	$-CO_2H$	$-CONH_2$	$-OCOR$
	τ for $\underline{H}-C-X$	7.9–8.0	7.43–7.93	7.98	5.0–6.35

6. Test for carbohydrates. Treat 0.1 g of the sample with 5 ml of water and 2 drops of a strong solution of α-naphthol in alcohol; then add 5 ml of conc. H_2SO_4 down the side of the tube so that it forms a lower layer. A red ring between layers and a deep violet color in the solution after the layers are mixed indicates the presence of a carbohydrate. Some polyhydroxy acids and some unsaturated aldehydes will also give a positive test in this reaction.

7. Test for amines. The presence of nitrogen in the sample should be verified first by a sodium fusion test.

a. Primary amines: To 5 ml of water, add 1–2 drops of the sample to be tested. If necessary, 1–2 drops of conc. hydrochloric acid may be added to dissolve the sample. Add 0.5 ml of the resulting amine solution to 3 ml of the 5-nitrosalicylaldehyde reagent. A copious precipitate within 2–3 min is a positive test for a primary amine. The appearance of a slight turbidity is not a positive test; it indicates that traces of primary amine may be present as impurities. Try the test on any primary amine available, except methylamine, for comparison.

b. Secondary amines: To 5 ml of water, add 1–2 drops of the sample to be tested. If necessary, 1–2 drops of conc. hydrochloric acid may be added to dissolve the sample. To 1 ml of the nickel chloride-carbon disulfide reagent, add 0.5–1 ml of conc. ammonia, followed by 0.5–1 ml of amine solution. A definite precipitate indicates a secondary amine. A slight turbidity reveals a trace of a secondary amine as an impurity. Try the test on any secondary amine for comparison.

c. Tertiary amines: If the substance is basic in water solution but is not a primary or secondary amine, assume that it is a tertiary amine.

d. Test for primary aromatic amines: To an ice-cold solution of the sample in 1.0 *N* HCl, add a saturated sodium nitrite solution, drop by drop, until it gives an immediate reaction to starch-iodide paper. Add a few drops to an alkaline solution of α-naphthol. An intensely colored mixture indicates an aromatic primary amine.

e. Test for primary aliphatic amines: To a suspension of 1 drop of sample in 5 ml of water, add 1 ml of acetone and 1 drop of a 1% solution of sodium nitroprusside. Development of a violet-red color within 2 min is a positive test.

SPECTRAL CHARACTERISTICS

Infrared

Pyrrole ν_{N-H} 3500 cm^{-1} $\nu_{N-H\cdots N}$ 3425 cm^{-1}
Arom ν_{C-N} primary 1250–1340
secondary 1280–1350
tertiary 1310–1360

n.m.r.

τ for $\underline{H}$—C—N 7.13–7.85

8. Test for aromatic nuclei. Sublime some dry aluminum chloride in a slanted test tube so as to form a heavy coat on the upper surface of the tube. Cool it, and add a drop of a solution containing 1 drop of sample in 1 ml of $CHCl_3$. Stopper the tube and let the solution come in contact with the film of $AlCl_3$. Aliphatic compounds give no color or are light yellow, and benzene derivatives give orange to red colors. Naphthalene gives a blue color, biphenyl purple, and anthracene green.

Infrared: (Benzene derivatives)
Two peaks near 1480 *and* 1625 cm^{-1}; both must be present.
Arom. ν_{C-H} 3030 cm^{-1} Ortho substitution, 735–770 cm^{-1}
Meta substitution 750–810
Para substitution 800–860

n.m.r.:

τ = 1–3.58

9. Test for nitro compounds. Add about 10 mg of the sample to 1 ml of ferrous sulfate reagent in a test tube, and then add 0.6 ml of alcoholic potassium hydroxide solution. Insert a glass tube so that it reaches the bottom of the test tube; then pass a stream of nitrogen gas through the tube for about 30 sec to remove air. Stopper the tube quickly and shake it. Note the color of the precipitate after 1 min. A positive test is indicated by the formation of a red-brown precipitate. A negative test is shown by a greenish precipitate. Nitroso compounds, quinone, alkyl nitrates, and alkyl nitrites also give a positive test.

	RNO_2	ϕNO_2
Infrared	1315–1390 cm^{-1}	1340–1355 cm^{-1}
	and	*and*
	1535–1610	1510–1550

10. Test for ethers. Mix 0.5 ml of the sample, 2 ml of glacial acetic acid, and 0.5 ml of conc. H_2SO_4. Reflux the contents 5 min, cool, and dilute with 5 ml of ice water. Test a drop of oily layer or benzene extract for ester by the test for acyl compounds.

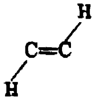
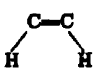
Infrared		ν_{C-O-C}
	Diaryl	1060–1150 cm^{-1}
	Dialkyl or arylalkyl	1230–1270

n.m.r.	$R—C\underline{H}_2OR$	$R—C\underline{H}_2O\phi$
τ =	6.60	6.10

11. Test for unsaturation. *a. Bromine in CCl_4:* Dissolve 2–3 crystals or 4–5 drops of the unknown in 2 ml of CCl_4, and add a 5% solution of bromine in CCl_4 drop by drop, with shaking, until the bromine color persists for about 1 minute. Blow across the top of the test tube or bring up an open bottle of ammonia to detect any HBr evolution.

b. Baeyer test: Dissolve 2–3 crystals or 4–5 drops of the sample in 2 ml of water or alcohol, and add a 2% aq. solution of $KMnO_4$ drop by drop until the pink color persists, or until 30 drops of the reagent are added. If only 3 drops of the reagent are decolorized, the test is negative.

c. Test for 1-alkynes: In a thoroughly clean test tube, prepare an ammoniacal silver nitrate solution as in test 1a with Tollens' reagent. Now add 3–4 drops or crystals of the unknown, and shake vigorously. The formation of a solid indicates a 1-alkyne (in the absence of an aldehyde or α-hydroxy ketone).

Infared		SPECTRAL CHARACTERISTICS		
	$\nu_{C=C}$	1620–1680 cm^{-1}	$\nu_{C\equiv C}$	2100–2140 cm^{-1}
Conj. ϕ, C=C, or C=O	$\nu_{C=C}$	1600–1625	$\nu_{\equiv C-H}$	3300
trans		960–990	$\nu_{=C-H}$	3080
cis		680–725	Sat. ν_{C-H}	2850–2970
	$H_2C=CR_2$	905–915		

Ultraviolet

$C{=}C\ \lambda_m = 185\ m\mu$ $C{=}C{-}C{=}C\ \lambda_m = 217\ m\mu$

n.m.r.

	τ *Unconjugated*	τ *Conjugated*
$R_2C{=}CH\underline{R}$	3.8–5.4	
$R_2C{=}C\underline{H}_2$	5.2–5.35	5.10
Cyclic $C{=}C\underline{H}$	4.1–4.7	4.1–4.6
$RC{\equiv}C{-}\underline{H}$	7.65	7.30
$R{-}C\underline{H}_3$	9.06–9.12	
$R_2C{=}C(C\underline{H}_3)_2$	8.3	

12. Test for salts. The sample should not be soluble in ether. Treat about 0.1 g of the finely divided sample with a few drops of 6 *N* NaOH on a watch glass, and note any odor which is produced. An ammoniacal or fishlike odor indicates that the substance is a salt of an amine or ammonia. Amides and nitriles may interfere with this test.

If the unknown is not a nitrogenous salt, add a few drops of conc. H_2SO_4 to a few crystals on a watch glass, and note any odor that is produced. A flocculent precipitate or a pungent odor suggests the liberation of a carboxylic acid from its salt.

For further confirmation, a larger sample may be used, and the amine or carboxylic acid produced for characterization.

Discussion. The test for a carbonyl compound consists of forming a 2,4-dinitrophenylhydrazone, which for most carbonyl compounds is very insoluble. Aldehydes are distinguished from ketones by their reduction of Tollens' reagent. Only aliphatic aldehydes reduce Benedict's reagent (alkaline copper citrate).

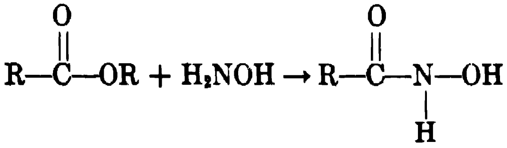
Ferric chloride in solution gives colors with a number of organic derivatives. The common ones are phenols, enols, oximes, and hydroxamic acids. However, the appearence of a color depends on such factors as the solvent, acidity, and concentrations of reactants. For example, the colors produced by 2-amino-5-nitrophenol in different solvents are as follows:

Solvent	*Color*
Water	Negative
Aqueous $NaHCO_3$	Brown
Methanol	Brown
Methanol-$NaHCO_{3\,aq}$	Red
Methanol-pyridine	Red
Chloroform	Green
Chloroform-pyridine	Brown
Diethylene glycol diethyl ether	Orange

The procedure given above in test 2 is generally satisfactory.

The textbook test for alcohols with sodium metal is impractical because it can be applied only when the sample is reasonably dry. If water were present in a sample, hydrogen gas would be evolved, although the sample may not be an alcohol. The test given here is based on the formation of a red-colored complex ion involving ceric ion and the alcohol. Aliphatic hydroxy compounds containing less than 10 carbon atoms have been tested with positive results. Aromatic amines and phenols interfere by forming deep colors and precipitates. Easily oxidized materials such as oxalic acid may interfere by decolorizing the test reagent before the red color of the test can be developed.[6] The Lucas test for distinguishing primary, secondary, and tertiary alcohols was discussed in Section 10.6c. This test is fairly reliable, although allyl, benzyl, and cinnamyl alcohols behave like tertiary alcohols. The test with permanganate is quite good. The tertiary alcohol is the hardest to oxidize and resists oxidation in glacial acetic acid. In this solvent, a primary alcohol is oxidized to an acid, and a secondary alcohol to a ketone. Then, when sulfuric acid is added, only the ketone from the secondary alcohol is oxidized.

The test for acyl compounds is based on the formation of a hydroxamic acid from any of the acyl compounds, esters, acid halides, etc.



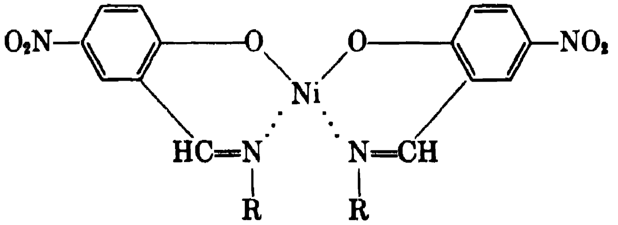
$$R-\overset{\overset{\displaystyle O}{\|}}{C}-OR + H_2NOH \rightarrow R-\overset{\overset{\displaystyle O}{\|}}{C}-\underset{\underset{\displaystyle H}{|}}{N}-OH$$

A hydroxamic acid

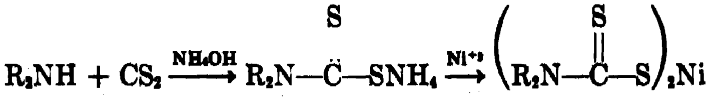
This gives a deep coloration with aq. Fe^{+3} ion, owing to the formation of a chelated complex.

The test for carbohydrates, the Molisch test, is believed to be based on the formation of a triphenylmethane-type dye between α-naphthol and a furfural.

The test for primary amines is based on the formation of a Schiff base between the 5-nitrosalicylaldehyde and the amine, which then forms a very insoluble nickel chelate.



Without the primary amine to form the Schiff base, the insoluble chelate would not be formed. The test for the secondary amine is based on the formation of an insoluble nickel compound:

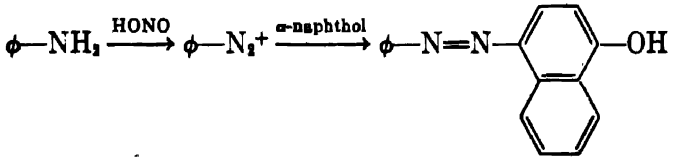


$$R_2NH + CS_2 \xrightarrow{NH_4OH} R_2N-\overset{\displaystyle S}{\ddot{C}}-SNH_4 \xrightarrow{Ni^{+2}} \left(R_2N-\overset{\overset{\displaystyle S}{\|}}{C}-S\right)_2Ni$$

---

[6] F. R. Duke and G. F. Smith, *Ind. and Eng. Chem., Anal. Ed.*, **12**, 201 (1940).

The test for the primary aromatic amine is based on diazotization of the amine, and coupling of the corresponding diazonium ion with α-naphthol to give a red azo-type dye (cf. page 411):



The chemistry of the test for aliphatic primary amines is not clearly known.

The test for aromatic nuclei is based on the formation of a colored complex ion between $AlCl_3$, $CHCl_3$, and the aromatic sample.

The test for nitro compounds is based on the oxidation of ferrous ion to ferric hydroxide, which is reddish-brown.

The test for an ether involves its hydrolysis to an alcohol, and esterification of acetic acid by the alcohol.

$$R_2O + 2AcOH \xrightarrow{H_2SO_4} 2AcOR + HOH$$

Then, the presence of an ester is verified by the acyl test. The chemistry of the rest of the tests given above has been discussed several times. The test for a salt involves liberation of the amine, if a salt of an amine, or liberation of the acid, if a salt of an acid.

21.2 RESOLUTION OF MIXTURES

Surprisingly, students find difficulty in making clear-cut resolutions of certain mixtures. For this reason, a general discussion of this common laboratory operation is given here.

The resolution of mixtures follows the same general procedure whether the identities of the components are known or unknown. The mixture is first examined for water solubility of one or more of the components. This would include the first few members of the aliphatic alcohols, aldehydes, amides, acids, and amines; acetone; sulfonic acids; carbohydrates; and salts. If the mixture is known to contain substances which react readily with water, this step would not be done. Most compounds which are insoluble in water will dissolve in ether. After water extraction, the mixture is taken up in ether. Occasionally, benzene or chloroform are used instead of ether. A solvent is used primarily for the purpose of working with a homogeneous mixture and for efficiency. Next, basic compounds are removed by extracting the ether solution with dilute mineral acid. Bases would form salts, and since most salts are water-soluble and ether-insoluble, the bases would enter the aqueous phase in the form of their salts. The aqueous phase would then be treated with aq. NaOH or Na_2CO_3 to liberate the organic bases. They could then be separated from the alkaline aqueous phase mechanically if insoluble, or isolated by $CHCl_3$ extraction. If there is a mixture of amines among the bases just isolated, a Hinsberg separation could be performed.

The organic acids are next extracted with dilute sodium hydroxide from the first ether solution of the original mixture. The layers are separated, and the organic acids regenerated by acidification of the alkaline solution. The organic acids are then isolated mechanically (i.e., filtration if a solid, or with a separatory funnel if a liquid) or by extraction. If weak and strong acids are present in the mixture of acids, they may be separated by extraction with aq. $NaHCO_3$. This would dissolve the acids stronger than phenol which may then be regenerated by acidifying the bicarbonate solution.

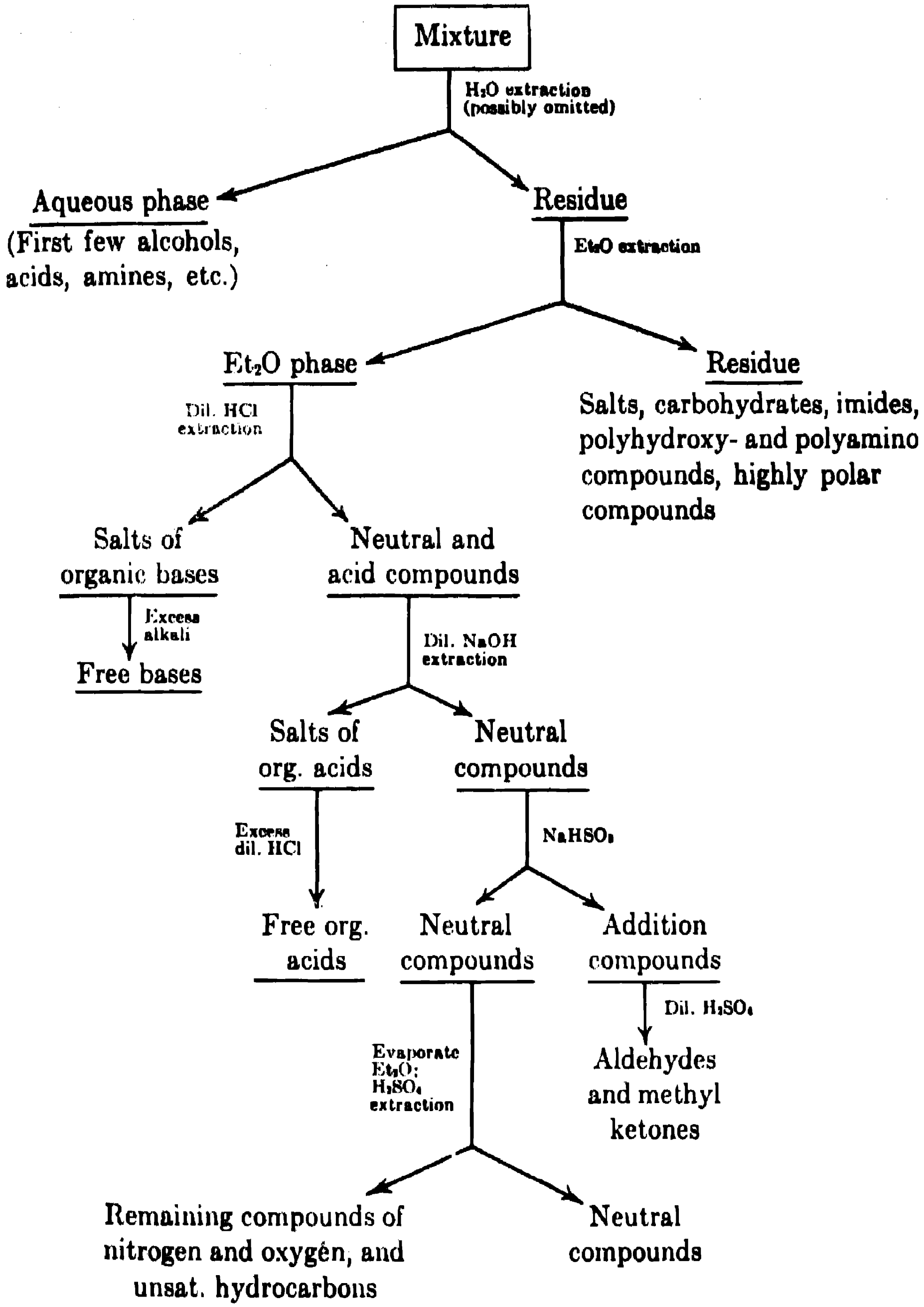
Only neutral components of the original mixture remain in the ether phase. Aldehydes and methyl ketones may be precipitated in the form of their bisulfite addition compounds by treatment with a saturated sodium bisulfite solution. After filtration, the aldehydes or methyl ketones are regenerated by decomposing the bisulfite addition compounds with dilute mineral acid.

The ether is now distilled from the remaining mixture. Extraction of the residue with cold concentrated sulfuric acid would remove unsaturated hydrocarbons, amides, and remaining oxygen-containing compounds, such as esters, ketones, alcohols, etc. Left behind would be saturated and aromatic hydrocarbons and saturated halides. Resolution of these two groups would have to be made either by a physical fractionating process (distillation, crystallization, chromatography), through inclusion complex formation, or with the use of several acid solvents differing in acidity, such as phosphoric acid and hydrogen fluoride. These finer separations are not commonly made in the elementary course and will not be discussed.

Steam distillation can sometimes be used instead of ether extractions. Thus, neutral and basic substances, but not acids, are ether extractable or steam distillable from aqueous basic solutions. Neutral and acidic substances, but not bases, are ether extractable or steam distillable from aqueous acid solutions.

Essentially, the procedure just outlined amounts to removing acidic substances from an ether solution of the mixture by alkali extraction and removing basic substances by an aqueous acid extraction. Then, if necessary, the amines are separated by the Hinsberg method, the acids are separated by steam distillation or weak base extraction, and the neutral substances are separated by bisulfite addition compound formation, by inclusion compound formation, or by sulfuric acid extraction. The important points to bear in mind are (1) salts are normally water-soluble, ether-insoluble, and nonvolatile; (2) bases form salts with acids and therefore cannot be distilled or extracted from mineral acid solution; and (3) organic acids form salts with alkali and hence cannot be distilled or extracted from alkaline solutions.

This resolution procedure can be diagramed as follows:


Mixture
H_2O extraction (possibly omitted)
Aqueous phase
(First few alcohols, acids, amines, etc.)
Residue
Et_2O extraction
Et_2O phase
Residue
Salts, carbohydrates, imides, polyhydroxy- and polyamino compounds, highly polar compounds
Dil. HCl extraction
Salts of organic bases
Neutral and acid compounds
Excess alkali
Free bases
Dil. NaOH extraction
Salts of org. acids
Neutral compounds
Excess dil. HCl
$NaHSO_3$
Free org. acids
Neutral compounds
Addition compounds
Dil. H_2SO_4
Aldehydes and methyl ketones
Evaporate Et_2O; H_2SO_4 extraction
Remaining compounds of nitrogen and oxygen, and unsat. hydrocarbons
Neutral compounds

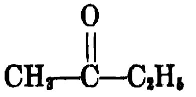
21.3 SPECTRA-STRUCTURE RELATIONSHIPS[6]

It is beyond the scope of this book to give more than a superficial discussion on the relationships between spectra and molecular structure. Some of the fundamental features of spectra and their origin were given in Chapter 6. It has been observed that in particular, resonance, hydrogen bonding, electronegativity, polarization, solvation, and steric requirements have a marked influence on spectra. Some of these effects will be illustrated here with regard to infrared, ultraviolet, and n.m.r. spectra.

---

[6] L. N. Ferguson, *The Modern Structural Theory of Organic Chemistry*, Prentice-Hall, Inc., Englewood Cliffs, N.J., 1963, Chapter 5.

a. Resonance. The typical infrared and ultraviolet absorption regions for the common type bonds were given in Chapter 6. The effect of resonance on spectra is revealed by a shift in the typical absorption ranges for the bonds involved. For illustration, the isolated C═O and C═C infrared frequencies for methyl ethyl ketone and 1-butene are

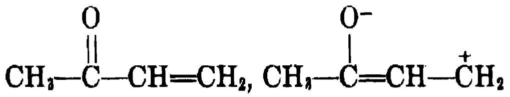


$$CH_3-\overset{O}{\overset{\|}{C}}-C_2H_5$$

$CH_3-CH_2-CH=CH_2$

$\nu_{C=O} = 1720\ cm^{-1}$ $\nu_{C=C} = 1647\ cm^{-1}$

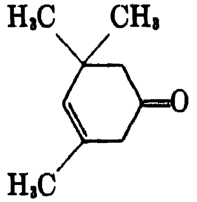
When these groups are conjugated, thereby increasing the contribution of the polar structures to the actual structures of the molecules,



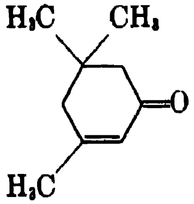
$$CH_3-\overset{O}{\overset{\|}{C}}-CH=CH_2,\quad CH_3-\overset{O^-}{\overset{|}{C}}=CH-\overset{+}{C}H_2$$

$\nu_{C=O} = 1685\ cm^{-1}$
$\nu_{C=C} = 1623$

the carbonyl and olefin bonds have less double-bond character, and hence the respective infrared frequencies shift toward the single-bond values. Increased resonance among polar structures also changes the wavelengths of the UV absorption bands:



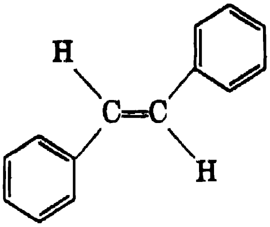
$\nu_{C=O} = 1725\ cm^{-1}$
$\lambda_m = 286\ m\mu$



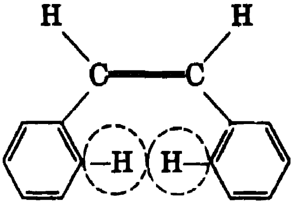
$\nu_{C=O} = 1672\ cm^{-1}$
$\lambda_m = 336\ m\mu$

Other examples of the effect of resonance of conjugated systems on UV spectra were given in Section 6.5.

b. Steric inhibition of conjugation. If steric requirements hinder or prevent the planarity required for resonance, then effects of resonance on spectra will be absent or diminished. Consequently, steric hindrance usually decreases λ_m in UV spectra, although there are certain explainable exceptions. For illustration, λ_m for *trans*- stilbenes and azobenzenes are larger than for the *cis* isomers.

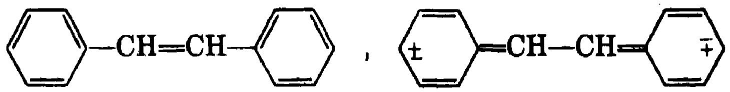


λ_m = 295 mμ

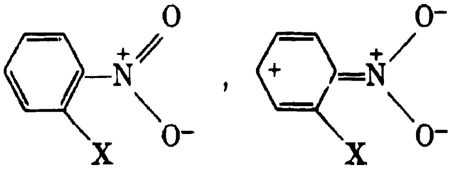


λ_m = 280 mμ

In the *cis* isomer, the ortho H's would overlap in a planar structure, and consequently, one benzene ring rotates out of the plane of the C=C bond. Planarity is necessary, however, for maximum resonance of the type

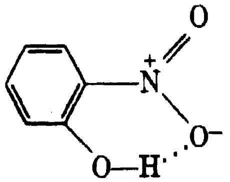


Similarly, ortho groups hinder the phenyl-nitro group resonance and λ_m for

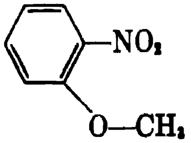


o-halonitrobenzenes decrease in the order of the sizes from the halogen atoms F > Cl > Br > I because of increased hindrance from the halogen atoms, to a planar nitrobenzene molecule.

c. Hydrogen bonding. In general, the effects of hydrogen bonding on UV spectra are noted by measuring the spectral differences between corresponding hydroxy and ether compounds or between ortho and para isomers of phenols. Intramolecular hydrogen bonding has a visible effect on UV spectra. For example, *o*-nitrophenol is yellow, but the methyl ether and *p*-nitrophenol are almost colorless.

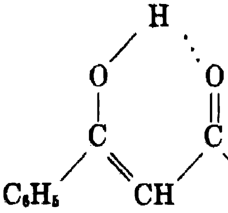


λ_m = 271 mμ

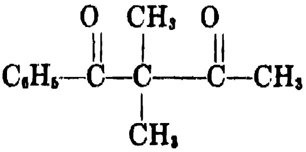


λ_m = 248 mμ

Hydrogen bonding makes it easier for the respective bonds to vibrate, and hence the corresponding infrared absorption frequencies are lowered. This was demonstrated in Section 10.5 for intermolecular and intramolecular hydrogen bonds. As another example, the C=O and O—H frequencies in benzoylacetone, $C_6H_5—CO—CH_2—COCH_3$, are lower than in the α,α-dimethyl derivative because the former compound enolizes and forms an intramolecular hydrogen bond:



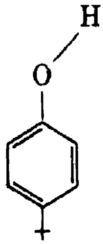
$\nu_{C=O}$ = 1603 cm^{-1}
ν_{O-H} = 2460–2520



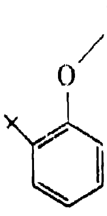
(Does not enolize)
$\nu_{C=O}$ = 1748, 1718 cm^{-1}
no ν_{O-H}

Steric hindrance to hydrogen bonding nullifies the spectral effect of a hydrogen bond. For example, *p*-*t*-butylphenol has a single infrared O—H band at 3608 cm^{-1} attributed to an associated state through intermolecular hydrogen bonds. The ortho isomer has two bands because some of the molecules are associated and some are monomeric. The, 2,6-di-*t*-butylphenol, on the other hand, is monomeric because the large *t*-butyl groups prevent the OH groups on different molecules from getting close enough to form a hydrogen bond. Thus, the infrared spectrum can often be used to detect hydrogen bonding or provide information about the spatial conditions within molecules.

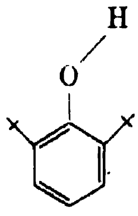
+ = *t*-butyl group:



p-*t*-Butyl phenol
Associated
ν_{O-H} = 3608 cm^{-1}

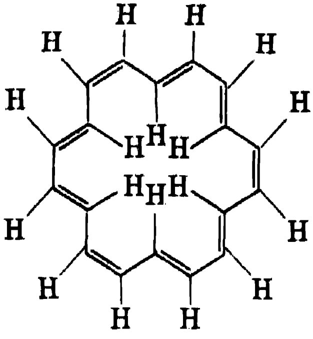


o-*t*-Butylphenol
Part associated,
part monomeric
ν_{O-H} = 3605, 3643 cm^{-1}



2,6-Di-*t*-butylphenol
Monomeric
ν_{O-H} = 3643 cm^{-1}

d. Aromatic rings. Nuclear magnetic resonance spectroscopy has become a very powerful diagnostic tool for structure elucidation and is useful for detecting aromatic rings. Aromatic protons lying outside of the π-electron "ring current" of an aromatic ring are deshielded and exhibit n.m.r. signals in the range τ = 1–3.5. On this basis, it was concluded that [18]annulene has an aromatic ring. It has two peaks, one at τ = 1.1 for the 12 peripheral protons and one at τ = 11.8 with half the former intensity for the six intraannular protons. In contrast to these values, the nonaromatic cyclooctatetraene exhibits one band at $\tau = 4.31$, outside of the aromatic range.



[18]Annulene

TEST QUESTIONS, Set 19

(For quantitative functional group analysis, see Sections A-3 and A-4 in the Appendix.)

1. An optically active amide *1* ($C_5H_{11}ON$) yields an acid and ammonia when hydrolyzed. When *1* undergoes the Hofmann degradation and the product is treated with nitrous acid, N_2 and an optically active alcohol are produced. The alcohol gives a positive iodoform test. What is the structure of *1*? Show how you reached your conclusion.

2. An unknown compound *2* ($C_{15}H_{11}O_5N$) gives a precipitate with 2,4-dinitrophenylhydrazine, does not reduce Tollens' reagent, and gives a bright red color when a solution in $CHCl_3$ is poured on sublimed $AlCl_3$. When *2* is heated with hydroxylamine hydrochloride in alcoholic KOH and then neutralized, the reaction mixture gives a blood-red color with aq. $FeCl_3$. Upon saponification and then acidification, two compounds *3* ($C_9H_8O_3$) and *4* ($C_6H_5O_3N$) are recovered. *4* gives a purple color with aq. $FeCl_3$, decolorizes a CCl_4 solution of Br_2 rapidly with the evolution of HBr, gives a brick-red color when treated with ferrous ammonium sulfate and alcoholic KOH in an oxygen-free vessel, and is steam distillable. *3* gives a precipitate with 2,4-dinitrophenylhydrazine, does not reduce Tollens' reagent, gives a positive iodoform test, and dissolves in alkali to be precipitated unchanged upon acidification. Upon oxidation of *3* with permanganate, the same acid, $C_8H_6O_4$, is obtained as results from the vigorous oxidation of naphthalene with permanganate. What is the structure of *2*? Show how you reached your conclusion.

3. A compound *5*, ($C_7H_6O_3$), reduces Tollens' reagent and gives a deep coloration with aq. $FeCl_3$. When 1.38 g of *5* are treated with excess acetic anhydride, 40 ml of 0.5 *N* NaOH are required to neutralize the liberated acid. What is a possible structural formula for *5*? What additional information would you need to determine the identity of *5*?

4. How could one separate and isolate the components in the following mixtures?

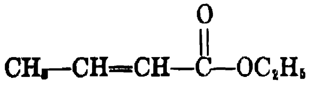
   (a) *o*-Nitrophenol, *p*-cresol, *p*-chlorobenzoic acid, N-methylaniline, N,N-diethylaniline, *p*-anisaldehyde (*p*-$CH_3OC_6H_4CHO$), and toluene.

   (b) Salicylaldehyde, *p*-hydroxybenzaldehyde, benzaldehyde, *d*- and *l*-mandelic acid ($C_6H_5CHOHCOOH$), pyridine, and chlorobenzene.

(c) *n*-Decane, isooctane (2,2,4-trimethylpentane), ethylene glycol, *n*-decanoic acid, and aniline.

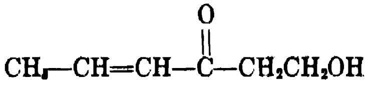
5. When phenol was chlorinated at a low temperature, two monochlorophenols were isolated. The infrared spectra of the products showed that A had two OH bands, one near 3620 cm^{-1} and one near 3590 cm^{-1}, whereas B had only one band near 3618 cm^{-1}. Assign structures to A and B and give the basis of your assignments.

6. What specific infrared absorption frequencies would you seek in order to distinguish the following three compounds:



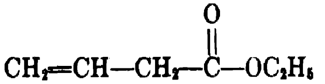
$CH_3{-}CH{=}CH{-}\overset{O}{\overset{\|}{C}}{-}OC_2H_5$

6



$CH_3{-}CH{=}CH{-}\overset{O}{\overset{\|}{C}}{-}CH_2CH_2OH$

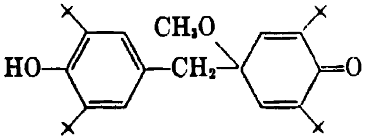
7



$CH_2{=}CH{-}CH_2{-}\overset{O}{\overset{\|}{C}}{-}OC_2H_5$

8

7. Structure *9* was assigned to a compound having the following spectral properties: UV: λ_m = 229 mμ; IR: ν = 1665, 1646, 3640, 1070 cm^{-1}. These spectral data support what structural features of *9*?

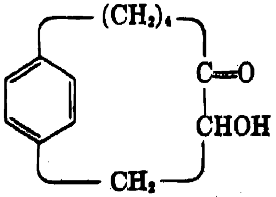


9

† = *t*-butyl group

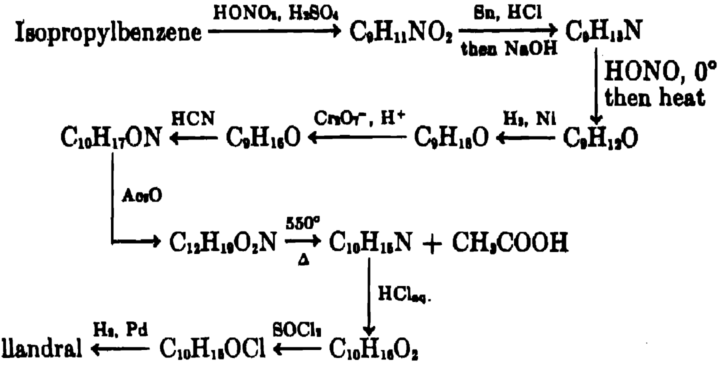
8. A compound *10*, $C_8H_{16}O_3$, liberates hydrogen when treated with sodium metal, is insoluble in alkali, and decolorizes cold dilute permanganate water. When *10* is reacted with $Pb(OAc)_4$, two compounds are obtained: *11*, $C_5H_{10}O_2$ and *12*, C_3H_4O. *12* reduces Tollens' reagent and decolorizes cold permanganate water. *11* does not reduce Tollens' reagent, forms a bisulfite addition compound, gives a positive iodoform test, gives a turbidity with Lucas reagent within 1 to 2 min, and liberates H_2 when treated with sodium metal. When *11* is heated with copper metal, a compound *13*, $C_5H_8O_2$, is isolated. *13* is soluble in aq. NaOH, gives a color with aq. $FeCl_3$, adds Br_2, and forms a semicarbazone. What is the structure of *10*? Show how you reached your conclusion.

9. When *14* was treated with Bi_2O_3 in hot acetic acid, two isomeric products, *15* and *16*, were obtained. *15* is yellow, m.p. = 110.5–112.5°, gives no immediate color with $FeCl_3$ in alcohol, has no IR band in the 3330–4000 cm^{-1} range but has a band at 1715 cm^{-1}. *16* is colorless, m.p. 98.5–100.5°, gives an immediate dark green color with $FeCl_3$, and has strong absorption bands in the IR at 3420, 1630, 1230 cm^{-1}, and a shoulder at 1655 cm^{-1}. Give probable structures for *15* and *16*.



14

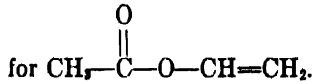
10. Deduce the structure of phellandral, $C_{10}H_{16}O$, a terpene found in eucalyptus oils, and predict λ_m and $\nu_{C=O}$ for it. (a) Phellandral reduces Tollens' reagent and cold, dilute permanganate solution. (b) Phellandral can be synthesized by the reaction sequence:



11. Identify the unknown compound **R** from the following data:

(a) Analysis: C, 63.1%; H, 5.26%; O, 31.64%.
(b) Mol. wt.: 152.
(c) **R** is soluble in alkali; gives no $FeCl_3$ test.
(d) Infrared absorption bands: 3250 (broad), 3030, 1700, 1625, 1480, 1230, 1100, 760 cm^{-1}.

12. Predict $\nu_{C=O}$ for



$CH_3—\overset{\overset{\displaystyle O}{\|}}{C}—O—CH{=}CH_2$.

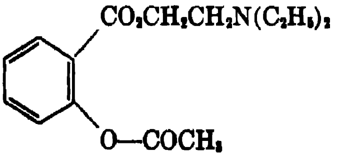
13. Based on solubility differences, how would you distinguish the members of each of the following pairs of compounds?

(a) $CH_3CH_2—CO—CH_2—CO_2C_2H_5$ and $CH_3—CO—CH_2CH_2—CO_2C_2H_5$.
(b) $CH_3—CO—CH_2CH_2CH_2—NHC_6H_5$ and $CH_3—CONH—CH_2CH_2CH_2C_6H_5$.
(c) p-$CH_3—C_6H_4—CH(NH_2)—C_6H_5$ and p-$CH_3—C_6H_4—NH—C_6H_5$.
(d) Glycerol and glycerol triethyl ether.
(e) Phthalimide and N-methylphthalimide.
(f) Sodium benzoate and benzoic acid.
(g) Sodium benzoate and sodium benzenesulfonate.

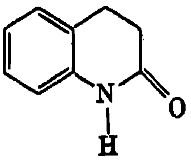
14. Write the structural formulas of the products that would be present after the hydrolysis of each of the following compounds in a 15% aqueous solution of sulfuric acid:

(a) $C_6H_5—CONH—CH_2—CONH_2$.
(b) $CH_3—(CH_2)_3—NH—CONH—CO—(CH_2)_3—CH_3$.
(c) $(C_2H_5)_2C{=}N—NHC_6H_5$

(d)



(e)



15. How would you distinguish the compounds in the following pairs by qualitative test tube experiments?

(a) *o*-Bromotoluene and benzyl bromide.
(b) Propylene glycol and trimethylene glycol.
(c) Isobutyl alcohol and isopropyl alcohol.
(d) 1,1-Diethoxyethane and 1,2-diethoxyethane.
(e) Phenylacetaldehyde and *p*-tolualdehyde.

16. An unknown compound ***17***, C_8H_8ClBr, is insoluble in conc. H_2SO_4 but quickly gives a precipitate when treated with alcoholic silver nitrate. When heated with an aqueous solution of sodium hydroxide, ***17*** is converted into ***18***, C_8H_9OBr, which is soluble in conc. H_2SO_4. Treatment of ***18*** with benzoyl chloride yields ***19***, $C_{15}H_{13}O_2Br$, and vigorous oxidation of ***18*** produces ***20***, $C_8H_5O_4Br$, which is soluble in dil. aq. NaOH and has a neutral equivalent of 121. ***20*** remains unchanged when heated. Give a possible structure for ***17*** and show how you reached your answer.

17. A compound ***21***, $C_{10}H_{14}O_2$, does not react with Tollens' solution, hot aq. NaOH, acetyl chloride, or sodium metal. Dilute hydrochloric acid changes ***21*** into ***22***, C_8H_8O, which does react with Tollens' reagent. Vigorous oxidation converts ***21*** and ***22*** into C_8H_6O, which loses water upon heating. What is a probable structure for ***21***?

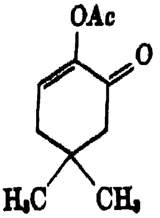
18. A compound ***23***, which contains nitrogen, is insoluble in water, but soluble in dilute acid and dilute alkali. It reacts with benzenesulfonyl chloride to give a product that is soluble in dilute alkali but insoluble in dil. acid. This latter compound has a neutral equivalent of 290. Compound ***23*** also reacts with benzoyl chloride to give a derivative with a neutral equivalent of 255. ***23*** does not evolve nitrogen when treated with nitrous acid, but reacts with bromine in carbon tetrachloride with the evolution of hydrogen bromide. What is a possible structure for ***23***?

19. A compound ***24***, $C_{11}H_8O_3NCl$, is insoluble in dil. acid and base, and does not react with 2,4-dinitrophenylhydrazine or acetyl chloride. Upon reduction with tin and hydrochloric acid, ***24*** is converted into ***25***, $C_{11}H_{10}ONCl$, which is soluble in dil. hydrochloric acid and liberates nitrogen upon treatment with nitrous acid. Vigorous oxidation of ***24*** yields ***26***, $C_9H_7O_7N$, which dissolves in dil. alkali, precipitates unchanged upon acidification, and has an equivalent weight of 121. Vigorous oxidation of ***24*** produces ***27***, $C_8H_5O_4Cl$, which is soluble in aq. alkali and has a neutral equivalent of about 101. ***26*** and ***27*** each lose a molecule of water when heated. Give a possible structure for ***24*** and show how you reached your answer.

20. Analysis, quantitative hydrogenation, and molecular weight measurements on a hydrocarbon ***28*** indicates it to be a cyclononatriene. It has the following spectral properties: IR: $\nu = 1615, 1647, 670$, and 717 cm^{-1}; UV: $\lambda_m = 223$ mμ, ϵ 3890; n.m.r.: $\tau = 4.23$, 7.4 ($C{=}C{-}CH_2{-}C{=}C$), and 7.96 ($C{=}C{-}CH_2$) in the ratio 3:1:2. Propose a structure for ***28*** and give the basis for your reply.

21. In the oligomerization of butadiene, a compound was obtained of b.p. 117°. Its analysis and molecular weight in benzene indicated a dimer of butadiene. It absorbed 3 moles of hydrogen. The infrared spectrum of the hydrogenated product is identical to that of 3-methylheptane. The UV spectrum of the dimer has a λ_m at 227 mμ, ϵ 25,100. Its CH_3 group gave a doublet ($\tau = 8.9$) in the n.m.r. Propose a structure for the dimer.

22. Three bottles each contain a different one of the following isomeric compounds:



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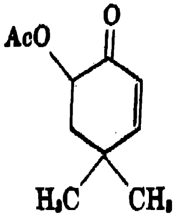

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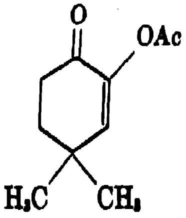

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On the basis of the following n.m.r. data, label the contents of each bottle: bottle 1, $\tau = 3.69$ (triplet), 7.61 (singlet), 7.63 (doublet); bottle 2, $\tau = 7.38$ (triplet), 8.13 (triplet), 3.85 (singlet); bottle 3, $\tau = 3.4$ (doublet), 4.23 (doublet), 4.64 (triplet), 7.93 (doublet).

22

Amino Acids and Proteins

22.1 THE NATURAL AMINO ACIDS

Amino acids are just what the name implies: molecules containing amino and acid groups. The most important ones are those in which the acid groups are carboxyl groups, and so this discussion shall be limited to the amino carboxylic acids.

The principal source of amino acids is from the hydrolysis of proteins. Proteins are high-molecular-weight substances found in all living tissue. Upon hydrolysis, they are broken up into thousands of amino acid molecules. However, only about 22 different types of amino acids have been isolated in this manner. Since these amino acids are obtained from living sources, they are referred to as *natural amino acids.* They can be named according to the Geneva system but are usually called by their common names. The structures, given in Table 22.1, need not be memorized other than, perhaps, that of

TABLE 22.1. NATURAL AMINO ACIDS[1]

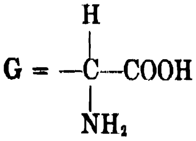
(See structures below)

Neutral		
Monoamino-monocarboxylic acid. . . .	1. Glycine	
	2. Alanine	
	3. Valine	
	4. Leucine	
	5. Isoleucine	
	6. Cysteine (Cystine)	. . . Sulfur containing
	7. Methionine	
	8. Serine	. . . Hydroxy
	9. Threonine	
Imino acids.	10. Hydroxyproline	. . . . Heterocyclic
	11. Proline	
Aromatic.	12. Phenylalanine	
	13. Tyrosine	
	14. Iodogorgoic acid	. . . . . Halogen containing
	15. Dibromotyrosine	
	16. Thyroxine	

[1] A few more may have been discovered, but as yet are not widely known.

TABLE 22.1. Continued

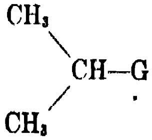
Basic	17. Tryptophane	Heterocyclic
	18. Histidine	
	19. Lysine	Diamino-monocarboxylic acid
	20. Arginine	
Acidic Monoamino-dicarboxylic acid	21. Aspartic acid	
	22. Glutamic acid	



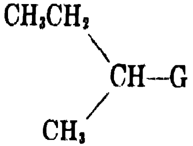
$$G = -\overset{\displaystyle H}{\underset{\displaystyle NH_2}{C}}-COOH$$

1. H—G

2. CH_3—G

3. 

4. $(CH_3)_2CH—CH_2—G$

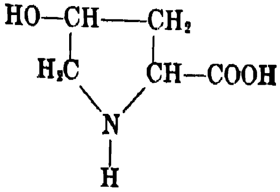
5. 

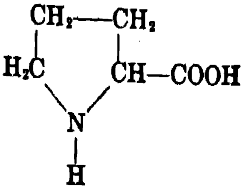
6. HS—CH_2—G(G—CH_2—S—S—CH_2—G)

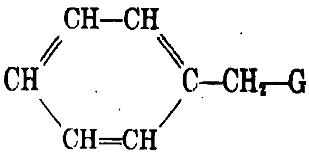
7. CH_3—S—CH_2CH_2—G

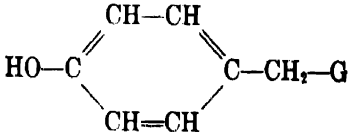
8. HO—CH_2—G

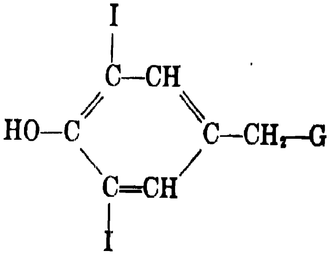
9. CH_3—CHOH—G

10. 

11. 

12. 

13. 

14. 

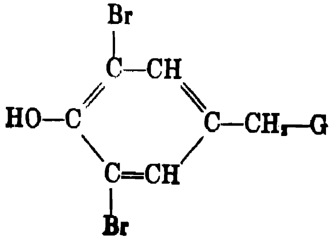
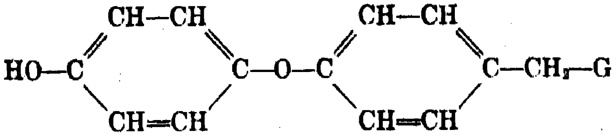
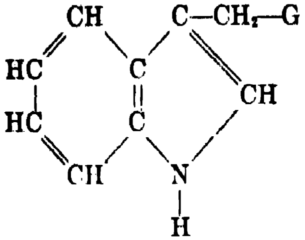
15. 

TABLE 22.1 Continued

16.

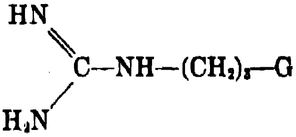


17.



19. $H_2N—(CH_2)_4—G$

20.

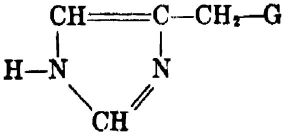


$$HN{=}C(—NH—(CH_2)_3—G)—H_2N$$

21. $HOOC—CH_2—G$

22. $HOOC—CH_2CH_2—G$

18.



glycine. They are given merely to reveal their similarities and differences.

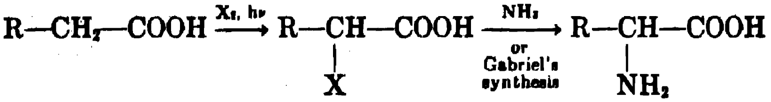
Of the natural amino acids, all but β-alanine, $H_2N—CH_2—CH_2—COOH$, are α-amino acids, and all of the α-amino acids are optically active (the α-carbon atom being asymmetric) except glycine. There are no storage depots in the body for amino acids; consequently the body must either synthesize them when needed or get them from the diet. The body can synthesize 12 of the natural amino acids; but, for normal growth and development, the other 10 have to be obtained from the proteins in our diet. These 10, therefore, are referred to as the *essential amino acids*. By convention, the natural optically active amino acids are designated *L* regardless of whether they are dextro- or levorotatory. For example, leucine and histidine as obtained from the hydrolysis of proteins are levorotatory and called *L*(−)-leucine and *L*(−)-histidine, respectively. The natural isomers of isoleucine and valine are dextrorotatory and called *L*(+)-isoleucine and *L*(+)-valine, respectively.

The hydrolysis of proteins to yield amino acids may be catalyzed by acid, alkali, or enzymes. When acid or enzyme catalysts are used, optically active amino acids may be recovered, but alkaline hydrolysis causes racemization of the optically active acids. The problem for a long time was the separation of the amino acids resulting from the hydrolysis of proteins. Usually fractional precipitation, or esterification followed by fractional distillation of the esters, was used. This required very tedious work and was inefficient. The development of chromatographic separations within the past 20 years—first column, then paper, and now vapor chromatography—has brought about a tremendous improvement in the ease and power of separating and isolating the amino acids.

22.2 SYNTHESIS OF AMINO ACIDS

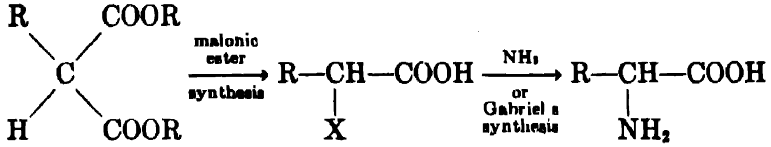
Many thousands of different amino acids can be synthesized if they are desired. Three common routes used are:

1. *Halogenation and aminolysis of acids*

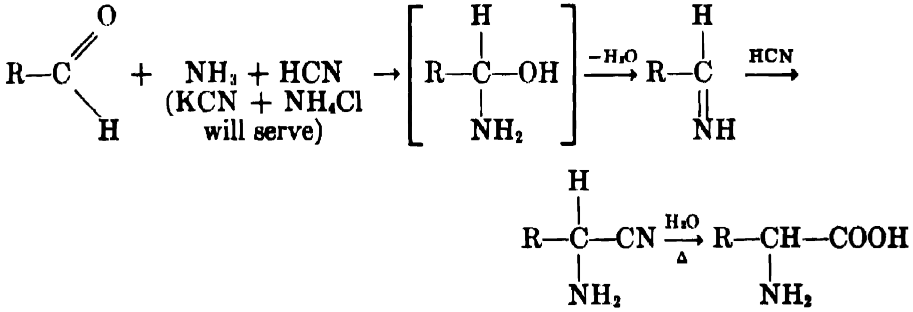


$$R{-}CH_2{-}COOH \xrightarrow{X_2,\ h\nu} R{-}\underset{\displaystyle X}{\underset{|}{C}}H{-}COOH \xrightarrow[\text{or Gabriel's synthesis}]{NH_3} R{-}\underset{\displaystyle NH_2}{\underset{|}{C}}H{-}COOH$$

2. *Malonic ester synthesis*

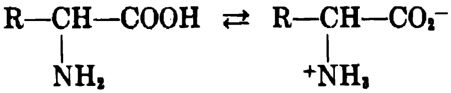


3. *Strecker reaction*



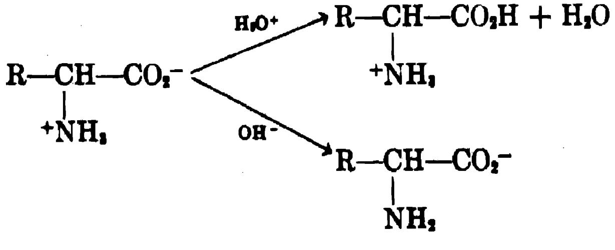
22.3 PHYSICAL PROPERTIES

Amino acids exist as an equilibrium mixture of a nonionic and a dipolar form:



$$R{-}\underset{\displaystyle NH_2}{\underset{|}{C}}H{-}COOH \rightleftarrows R{-}\underset{\displaystyle {}^{+}NH_3}{\underset{|}{C}}H{-}CO_2^-$$

The equilibrium lies somewhere on the right, so that amino acids exist over 50 per cent in the dipolar or *zwitterion* form. This gives them a saltlike character, as revealed by their large solubility in water and insolubility in ether and by their relatively high melting points. They are amphoteric and react as acids or bases:



In an electric field, amino acids migrate to the cathode in acid solutions and to the anode in basic solutions. For each amino acid, there is a definite *p*H at which the acidic and basic ionizations are equal, known as the *isoelectric point*. This point is seldom at neutrality, $pH = 7$, because the basic amino group may be more or less basic than the carboxyl group is acidic.

The solubility of an amino acid in water is minimum at its isoelectric point and often its isolation is attempted at this *p*H. Other properties are found to be at a minimum at the isoelectric point, such as the mobility, conductivity, osmotic pressure, viscosity, and stability toward coagulating agents. The minimum is sometimes quite sharp and therefore provides a means of determining the *p*H of the isoelectric point.

Other forms of evidence for the zwitterion form of amino acids are as follows:

(1) Heats of dissociation:

$$\text{R—COOH} + H_2O \rightleftharpoons RCO_2^- + H_3O^+ \qquad \Delta H \simeq 1000 \text{ cal/mole}$$

$$\text{R—NH}_3^+ + H_2O \rightleftharpoons \text{R—NH}_2 + H_3O^+ \qquad \Delta H \simeq 12{,}000 \text{ cal/mole}$$

The experimental heat of neutralization in acid media is -1300 to -2100 cal/mole; hence protons are combining with $—CO_2^-$ groups. In alkali, the heat of neutralization is 10,000 to 13,300 cal/mole, hence hydroxide ions react with ammonium groups.

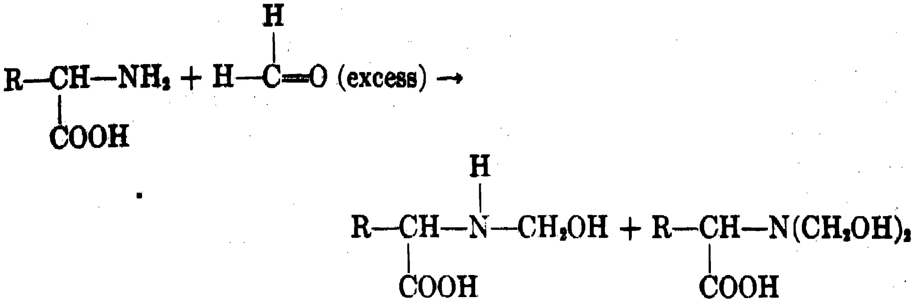
(2) Dipole moments and dielectric constants: the dipole moments of amino acids are very large, 10–15D, indicating a considerable ionic or dipolar character. Also, upon dissolution in water, they raise the dielectric constant of water, something done only by polar molecules.

(3) Raman spectra of neutral solutions indicate the presence of CO_2^- rather than COOH groups.

(4) There is an electrocontraction when amino acids are dissolved in water. For example, if 1 mole of glycol amide, $CH_2OH—CONH_2$, dissolves in a large volume of water, the volume increases 56.2 ml, but if isomeric glycine, $H_3N^+—CH_2CO_2^-$, is dissolved in the same volume of water, the volume increases only 43.5 ml. The dipolar glycine molecule attracts the polar H_2O molecules more strongly than glycol amide does, to give closer packing.

(5) The dissociation constants of amino acids correspond to those of NH_3^+ and CO_2^- rather than COOH and NH_2.

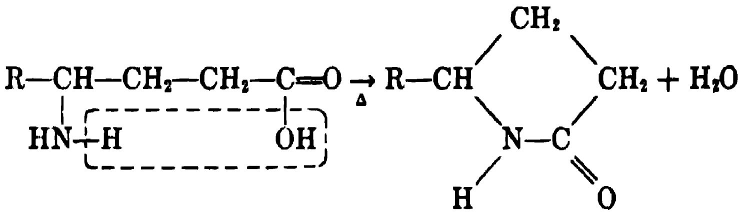
The basic and acidic groups of amino acids interfere in their titration, and prevent sharp end-points from being obtained. Sørensen, a Danish physical-biochemist who originated the use of the *p*H scale as a measure of acidity of solutions, found that the addition of a large excess of formaldehyde ties up amino groups, permitting the attainment of sharp end-points when titrating amino acids with alkali. Such a titration is called *formol titration*. One explanation is that the amino groups undergo hydroxymethylation to reduce the basicity of the nitrogen atom:



$$R-\underset{\substack{|\\ COOH}}{CH}-NH_2 + H-\overset{\substack{H\\ |}}{C}=O \text{ (excess)} \rightarrow R-\underset{\substack{|\\ COOH}}{CH}-\overset{\substack{H\\ |}}{N}-CH_2OH + R-\underset{\substack{|\\ COOH}}{CH}-N(CH_2OH)_2$$

22.4 CHEMICAL PROPERTIES

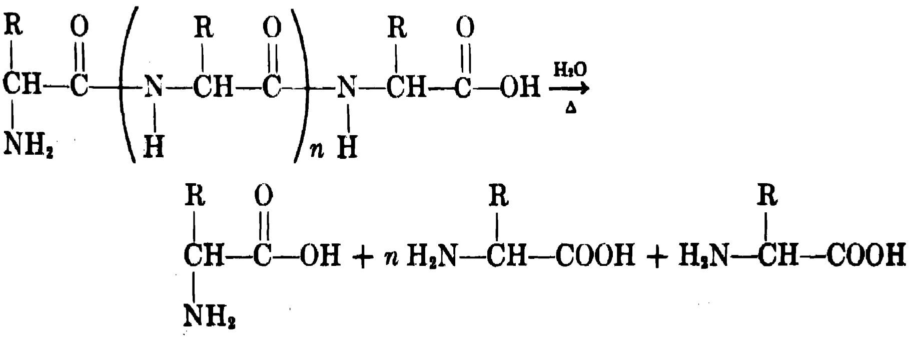
The amino acids undergo the general reactions of amines and of carboxylic acids. Thus, they react with nitrous acid and acetic anhydride as do amines, and they form the usual carboxyl derivatives, such as esters, amides, acid halides, etc. When the γ- and δ-amino acids are heated, they suffer the loss of H_2O to form *lactams*.



A lactam

22.5 POLYPEPTIDES

In 1902, Emil Fischer[2] and Franz Hofmeister independently proposed that proteins consist of chains of amino acids, and Fischer went on to accumulate convincing evidence. For example, he showed that proteins contain few free amino or carboxyl groups, but after hydrolysis, the reaction products contain many of these groups.

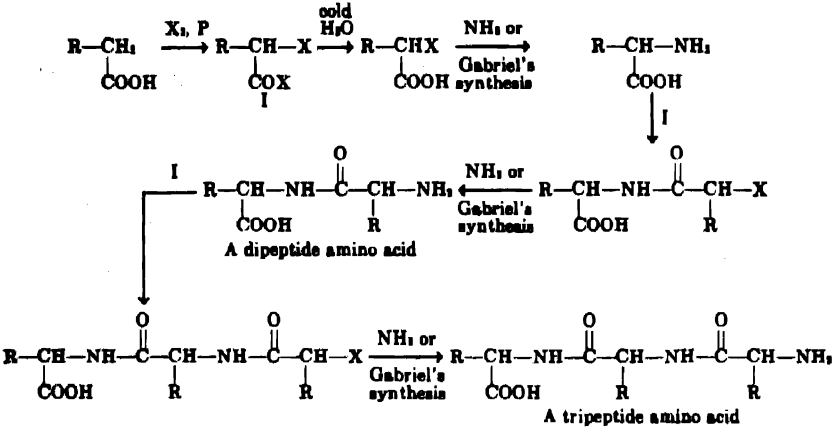


$$\underset{\substack{|\\ NH_2}}{\overset{\substack{R\\ |}}{CH}}-\overset{\substack{O\\ \|}}{C}-\left(\underset{\substack{|\\ H}}{N}-\overset{\substack{R\\ |}}{CH}-\overset{\substack{O\\ \|}}{C}\right)_n-\underset{\substack{|\\ H}}{N}-\overset{\substack{R\\ |}}{CH}-\overset{\substack{O\\ \|}}{C}-OH \xrightarrow[\Delta]{H_2O} \underset{\substack{|\\ NH_2}}{\overset{\substack{R\\ |}}{CH}}-\overset{\substack{O\\ \|}}{C}-OH + n\, H_2N-\overset{\substack{R\\ |}}{CH}-COOH + H_2N-\overset{\substack{R\\ |}}{CH}-COOH$$

---

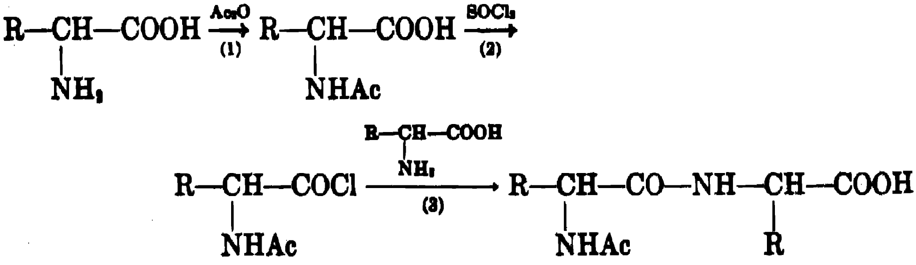
[2] Emil Fischer, a German organic chemist, received the Nobel Award in chemistry in 1902.

Fischer showed that compounds containing the amide grouping $-\overset{\overset{\displaystyle O}{\|}}{C}-\overset{|}{N}-$, called a *peptide bond*, give a coloration with alkaline copper sulfate (known as the Biuret test)—the more peptide links there are in a compound, the deeper the color. Proteins give dark violet colors, indicating the presence of many peptide groups. Finally, he synthesized a polypeptide by joining 18 amino acid molecules (15 of glycine and 3 of leucine). The product had a molecular weight over 1200, gave a positive Biuret test, and exhibited the Tyndall effect.[3] Fischer's synthesis was more elaborate than will be given here, but the following sequence brings out the important points in his preparation of a polypeptide.



When the two latter reactions are continued, amino acid units may be added one at a time to form a high-molecular-weight product.

Fischer's procedure added amino acid units to the amino group of the polypeptide chain. Another approach is to add them to the COOH group end.



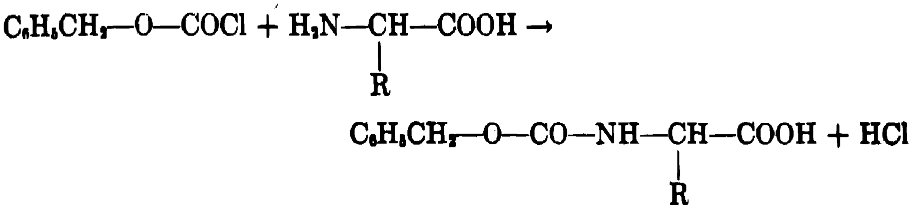
$$\underset{\displaystyle NH_2}{R-\underset{|}{C}H-COOH} \xrightarrow[(1)]{Ac_2O} \underset{\displaystyle NHAc}{R-\underset{|}{C}H-COOH} \xrightarrow[(2)]{SOCl_2}$$

$$\underset{\displaystyle NHAc}{R-\underset{|}{C}H-COCl} \xrightarrow[(3)]{R-CH(NH_2)-COOH} \underset{\displaystyle NHAc}{R-\underset{|}{C}H}-CO-NH-\underset{\displaystyle R}{\underset{|}{C}H}-COOH$$

---

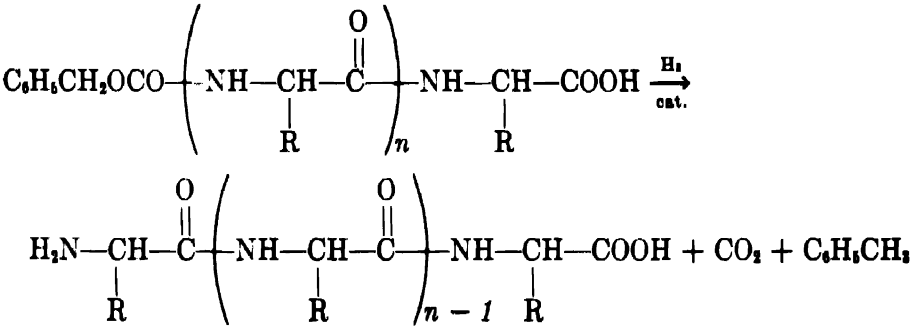
[3] When a light beam passes through an ordinary solution, its path cannot be seen, but when passing through a colloidal solution, its path can be seen just as a sunbeam is seen when shining into a dusty room. The dust particles reflect the light to reveal the light path. The small particles of a colloidal solution also reflect light to expose the light path. Large molecules frequently give colloidal solutions rather than dissolved molecules or ions, and the Tyndall effect is used as a means of detecting colloidal solutions.

Alternate repetition of steps (2) and (3) adds successively amino acid units. However, the initial acyl group used to protect the first NH_2 group can only be removed by hydrolysis. This would also hydrolyze all peptide links, resulting in a batch of amino acids. The problem was solved by using a protective group which may be removed through hydrogenation. Benzyl chloroformate (commonly called carbobenzoxy chloride) is first reacted with an amino acid.



$$C_6H_5CH_2{-}O{-}COCl + H_2N{-}\underset{\mathrm{R}}{\underset{|}{\mathrm{CH}}}{-}COOH \rightarrow C_6H_5CH_2{-}O{-}CO{-}NH{-}\underset{\mathrm{R}}{\underset{|}{\mathrm{CH}}}{-}COOH + HCl$$

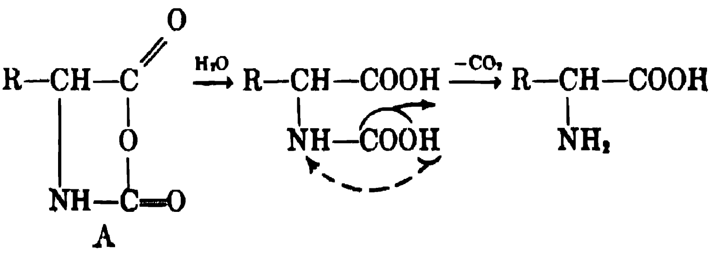
When steps (2) and (3) are used alternately, amino acid units may be added one at a time, different amino acids being used if desired, until a long-chain polypeptide has been formed. Then, the carbobenzoxy group may be removed by catalytic hydrogenation.



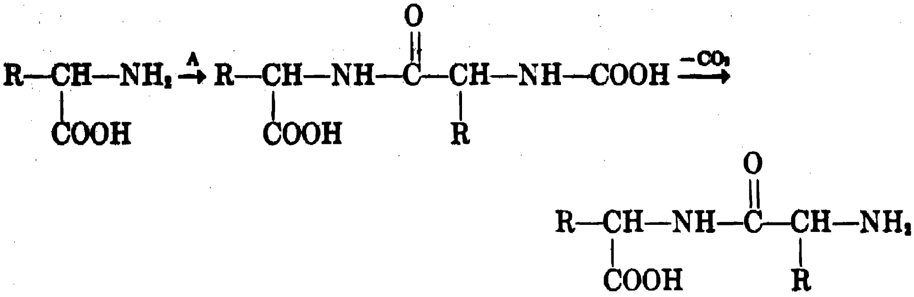
$$C_6H_5CH_2OCO\left(NH{-}\underset{\mathrm{R}}{\underset{|}{\mathrm{CH}}}{-}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\right)_n NH{-}\underset{\mathrm{R}}{\underset{|}{\mathrm{CH}}}{-}COOH \xrightarrow[\text{cat.}]{H_2}$$

$$H_2N{-}\underset{\mathrm{R}}{\underset{|}{\mathrm{CH}}}{-}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\left(NH{-}\underset{\mathrm{R}}{\underset{|}{\mathrm{CH}}}{-}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\right)_{n-1} NH{-}\underset{\mathrm{R}}{\underset{|}{\mathrm{CH}}}{-}COOH + CO_2 + C_6H_5CH_3$$

In recent years, polypeptides have been prepared by polycondensations. In the presence of a small amount of water, an N-carboxyanhydride (called Leuchs' anhydride) hydrolyzes, then suffers the loss of CO_2 to produce an amino acid.

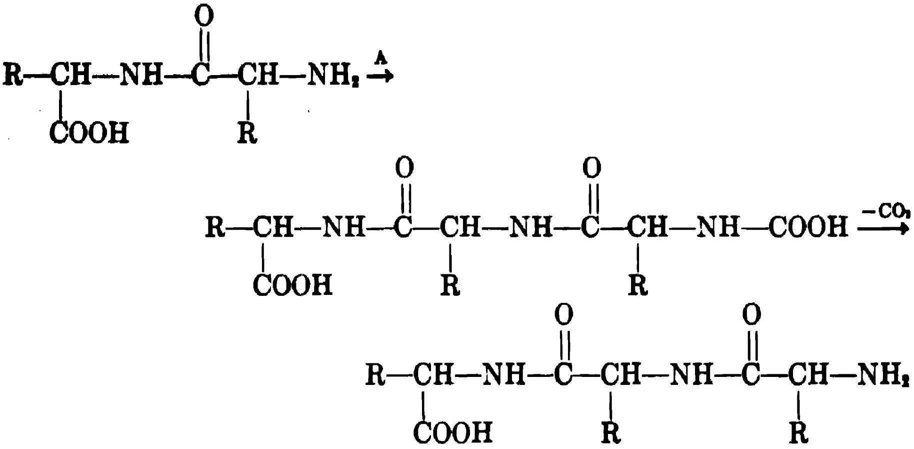


Then, more of the anhydride A quickly reacts with the amino group as any anhydride would. When this intermediate product loses CO_2, a dipeptide results.



$$\text{R—}\underset{\substack{|\\ \text{COOH}}}{\text{CH}}\text{—NH}_2 \xrightarrow{A} \text{R—}\underset{\substack{|\\ \text{COOH}}}{\text{CH}}\text{—NH—}\overset{\substack{\text{O}\\ \|}}{\text{C}}\text{—}\underset{\substack{|\\ \text{R}}}{\text{CH}}\text{—NH—COOH} \xrightarrow{-CO_2} \text{R—}\underset{\substack{|\\ \text{COOH}}}{\text{CH}}\text{—NH—}\overset{\substack{\text{O}\\ \|}}{\text{C}}\text{—}\underset{\substack{|\\ \text{R}}}{\text{CH}}\text{—NH}_2$$

Upon reaction with more of the anhydride and loss of CO_2, a tripeptide is produced.



$$\text{R—}\underset{\substack{|\\ \text{COOH}}}{\text{CH}}\text{—NH—}\overset{\substack{\text{O}\\ \|}}{\text{C}}\text{—}\underset{\substack{|\\ \text{R}}}{\text{CH}}\text{—NH}_2 \xrightarrow{A} \text{R—}\underset{\substack{|\\ \text{COOH}}}{\text{CH}}\text{—NH—}\overset{\substack{\text{O}\\ \|}}{\text{C}}\text{—}\underset{\substack{|\\ \text{R}}}{\text{CH}}\text{—NH—}\overset{\substack{\text{O}\\ \|}}{\text{C}}\text{—}\underset{\substack{|\\ \text{R}}}{\text{CH}}\text{—NH—COOH} \xrightarrow{-CO_2} \text{R—}\underset{\substack{|\\ \text{COOH}}}{\text{CH}}\text{—NH—}\overset{\substack{\text{O}\\ \|}}{\text{C}}\text{—}\underset{\substack{|\\ \text{R}}}{\text{CH}}\text{—NH—}\overset{\substack{\text{O}\\ \|}}{\text{C}}\text{—}\underset{\substack{|\\ \text{R}}}{\text{CH}}\text{—NH}_2$$

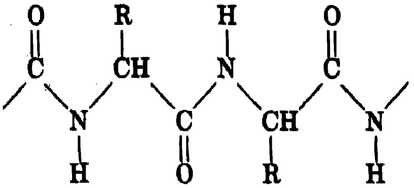
This sequence of reactions repeats itself until products of extremely high molecular weights (1 million to 15 million) result.

Similarly, amino acid chlorides may be polycondensed. An amino acid chloride hydrochloride salt, $\text{R—}\underset{\substack{|\\ \text{NH}_3\text{Cl}}}{\text{CH}}\text{—COCl}$, is prepared from the amino acid and PCl_5 and then purified with careful exclusion of moisture. When heated in a vacuum, or in basic media like triethylamine, the amino acid chloride polycondenses to polypeptides of 10 to 30 units.

22.6 PROTEINS AND NUCLEIC ACIDS

Proteins make up a large part of all living matter, comprising over half the solid substance in the tissues of man and other mammals, and play a central role in virtually all activities of living cells. Hair, nails, leather, skin, and flesh are mostly proteinic material. Proteins are responsible for the contraction of muscles, the protein hemoglobin carries oxygen from the lungs to the tissues throughout the body, and other enzymatic proteins control heredity. Consequently, proteins are extremely important to each of us and are of much interest to chemists.

It was indicated in Section 22.5 that proteins are built up from amino acids which have been united through the loss of water to form peptide bonds. The backbone of the polypeptide chain consists of the sequence



in which hundreds of amino acid units may be strung together in a single chain. The order and type of amino acids in the chain control the properties and biological functions of the protein. The amino acid format of natural proteins is much like words in a spoken language. In English, for instance, we have thousands of words made up from just 26 letters, but there are millions upon millions of nonwords possible from different combinations of these same letters. Similarly, there appears to be only a few thousand different natural proteins, although billions are possible from different combinations of the 22 different amino acids.

The order of amino acids in the protein structure is not the complete story. Each chain is coiled and attached to other chains through S—S and hydrogen bonds and ionic forces (see Figure 22.1) which gives the protein its *secondary* structure. Finally, the chains are coiled and folded in a three-dimensional pattern, called its *tertiary* structure, and held in this framework chiefly by hydrogen bonds. Nevertheless, the tertiary structure or topography of the protein, which determines its biological func-

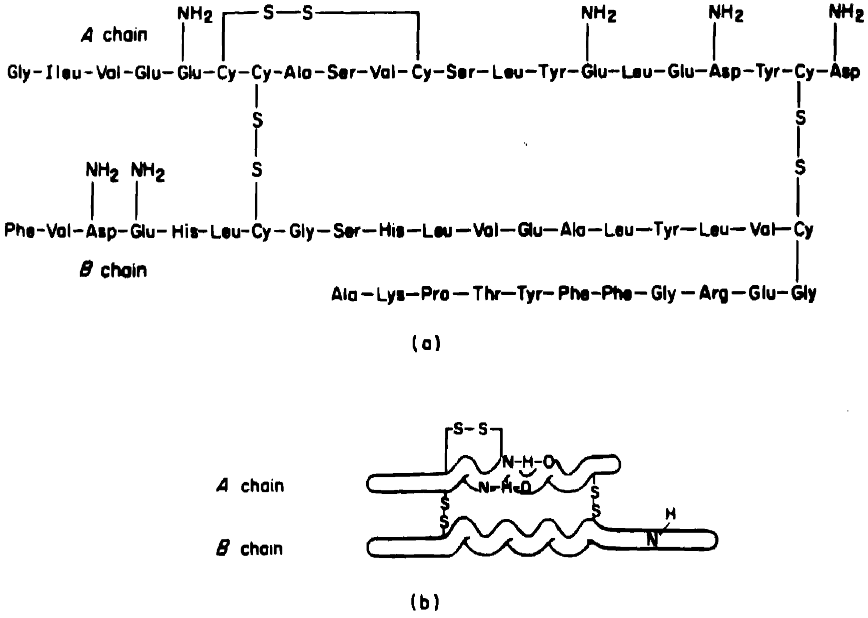

A chain
NH2
S—S
NH2
NH2
NH2
Gly-Ileu-Val-Glu-Glu-Cy-Cy-Ala-Ser-Val-Cy-Ser-Leu-Tyr-Glu-Leu-Glu-Asp-Tyr-Cy-Asp
S
S
S
S
NH2
NH2
Phe-Val-Asp-Glu-His-Leu-Cy-Gly-Ser-His-Leu-Val-Glu-Ala-Leu-Tyr-Leu-Val-Cy
B chain
Ala-Lys-Pro-Thr-Tyr-Phe-Phe-Gly-Arg-Glu-Gly
(a)
S-S
N-H-O
N-H-O
A chain
S
S
S
S
H
N
B chain
(b)

Fig. 22.1. The amino acid structure of insulin (a) and a schematic drawing of the possible coiling of a portion of the molecule showing its S-S and hydrogen bond secondary structure. Taken from A. P. Ryle, F. Sanger, L. F. Smith, and K. Kitai, *The Biochemical Journal*, **60**, 541 (1955).

tion, is fundamentally dependent upon the amino acid pattern in the chain. Denaturation of a protein consists in unfolding its tertiary structure, which may be reversible or irreversible, depending on the extent of derangement.

The name "protein," originated by the Swedish chemist Berzelius, was taken from the Greek word *proteios*, meaning "of the first order." But proteins are so complex in structure, so varied in molecular size and shape, composition and properties, that the Danish biochemist Linderstrøm-Lang thought of violating history and deriving their name from Proteus, the Greek god of the sea who could assume any shape he desired.

A protein may be hydrolyzed and its constituent amino acids identified to give its general composition. For example, the amino acid contents of three familiar proteins are given in Table 22.2. Owing to the difficulties in the analyses, the total percentages do not equal 100 exactly. The error in molecular weights may range from 3 to 15 per cent. These analyses, however, do not reveal the order in which the amino acids are connected in the polypeptide chain.

TABLE 22.2. AMINO ACID CONTENT OF SOME PROTEINS

Amino Acid	Hemoglobin, mol. wt. 68,000 %	Gelatin, mol. wt. 70,000 %	Egg Albumin, mol. wt. 44,000 %
Glycine	5.6	23.6	1.9
Alanine	7.4	10	7.4
Valine	9.1	2.5	6.8
Leucine	15.4	3.7	9.4
Isoleucine	0	1.7	
Phenylalanine	7.7	2	6
Tyrosine	3.0	0.2	4.2
Tryptophane	1.7	0	1.4
Serine	5.8	3.3	7.6
Threonine	4.4		
Cysteine	4.6		
Cystine	0.9	0.1	1.7
Methionine	1.0	0.8	5.0
Proline	3.9	15.3	4.5
Hydroxyproline		13	
Arginine	3.7	7.6	5.7
Histidine	8.7	1.0	1.8
Lysine	8.5	4.3	4.5
Aspartic acid	10.6	8.5	8.2
Glutamic acid	8.5	5.4	16.3

The first successful determination of the amino acid sequence in a natural protein was reported in 1954 by Frederick Sanger and his coworkers at Cambridge University.

Their success rested largely upon two advances in technique. One was the development of paper chromatography by two British chemists, A. J. P. Martin and R. L. M. Synge, for which they received the chemistry Nobel Award in 1952. The second key to Sanger's success was his discovery of the way to identify the amino acid at the end of a polypeptide chain. He found that a dinitrophenyl (DNP) group could be attached to the free amino group to form an easily identified compound. When the polypeptide is hydrolyzed into separate amino acid fragments, the DNP group remains attached to the unit formerly at the end of the polypeptide chain, and in this way the end amino acid group becomes identified. By cleaving a polypeptide randomly in various size fragments, identifying the end amino acid units of the various fragments, and noting overlapping sequences in the several fragments, Sanger and his group were able to deduce the complete succession of amino acids in the insulin molecule (51 amino acid units of 17 different types, mol. wt. 5,733; see Figure 22.1).

Sanger's epochal achievement triggered a wave of activity in this field. Other reactions were found for labeling end amino acids in polypeptide chains, and larger proteins were investigated. As a result, the amino acid structures have been determined for the following proteins:

Tobacco mosaic virus	158 amino acid units, mol. wt. 18,000
Ribonuclease	124 amino acid units of 17 different types, mol. wt. ca. 14,000
ACTH	39 amino acid units, mol. wt. 4,500
One of the chains in fetal hemoglobin	574 amino acid units
Glucagon, a pancreatic hormone	15 amino acid units, mol. wt. 3,485

During the period that Sanger was conducting his significant experiments in degrading the insulin protein molecule to ascertain its amino acid structure, an equally monumental program was underway in this country to synthesize a natural protein. V. du Vigneaud[4] and his associates at Cornell University synthesized a protein (oxytocin) which is identical structurally and biologically to the natural substance.

From an examination of the sequence of amino acids found so far in proteins, it is apparent that the order is random, and frequently an amino acid repeats itself in succession in the chain. Since only some 22 different amino acids are found in proteins, the mechanism of protein synthesis must be responsible for the arrangement of these 22 building blocks into the random but highly specific order in a given protein. A single alteration of one amino acid out of one or two hundred may give rise to a protein with a different biological activity. For example the hemoglobin S differs from normal hemoglobin by having a single valine amino acid unit in place of a single glutamic acid link in a 546-link chain. This gives the hemoglobin S different chemical, physical, and biological properties responsible for the disease called sickle cell anemia, characterized by the presence of sickle-shaped red blood cells. The disease can be mild or fatal.

Chemical methods can provide considerable information about the primary and secondary structures of proteins, but physical methods have been needed to ascertain their tertiary structures. Thus, by X-ray diffraction studies, Linus Pauling[5] and his coworkers at the California Institute of Technology determined the tertiary structure of fibrous proteins, and J. C. Kendrew and M. F. Perutz[6] determined the complete structure of the myoglobin molecule, which is responsible for muscle action.

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[4] Vincent du Vigneaud, an American biochemist, received the Nobel Award in chemistry in 1955.

[5] Linus Pauling, an American physical chemist, received the Nobel Prize in chemistry in 1954. When he was named winner of the 1962 Nobel Peace Prize, he was the only person to receive two such awards alone (Marie Curie won the 1911 chemistry Nobel Prize and shared the 1903 award in physics).

Proteins give various color reactions for their qualitative detection, the color depending upon the amino acids composing them. For example, proteins that contain tyrosine give a yellow color with concentrated nitric acid (the yellow-brown color produced when nitric acid is spilled on the skin), known as the xanthroproteic acid test. Also, they produce a blue color in alkaline phosphomolybdates, and a red color with Millon's reagent (a solution obtained by dissolving mercury in concentrated nitric acid and diluting with water).

Because of the presence of many ionizable amino and carboxyl groups, proteins are markedly affected by the *p*H of their environment. There is usually a definite *p*H at which each protein will exhibit its maximum biological activity; this *p*H is not necessarily its isoelectric point. Most heavy metal salts precipitate proteins, causing them to become denatured, i.e., lose their biological activity. Certain strong organic acids like trichloroacetic and picric acids form insoluble precipitates with proteins. Certain medical practices are based on this precipitation of proteins with reagents. For example, picric and tannic acids are used in salves or solutions for treating burns, because they precipitate proteins and form a protective coating. Egg albumin is administered in cases of heavy metal poisoning, because it forms a precipitate with the metal ions and prevents adsorption of the ions. The precipitate is removed from the stomach with a stomach pump or by vomiting. Proteins also form complexes with fats, called *lipoproteins*, and with large unsaturated compounds, as with retinene in visual purple of the eye.

a. Enzymes. Increasing the importance of proteins is the fact that enzymes are complex protein molecules also. Enzymes are catalysts for biological processes; indeed, there is no known biological process that is not started and directed in its course by enzymes. Breathing, muscular contractions, nerve impulses, and all biological actions are triggered by some specific enzyme.

The word comes from the Greek *zyme*, meaning leaven or "in yeast." In 1897 Eduard Buchner[7] ground up some yeast cells, squeezed out the juice, and obtained a solution which would also convert sugar into alcohol. Other scientists took up the difficult task of isolating a pure enzyme, and finally in 1926, James Sumner[8] at Cornell obtained a pure crystalline enzyme from jack bean which catalyzes the hydrolysis of urea.

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[6] J. C. Kendrew and M. F. Perutz, British physicists, received the Nobel Prize in chemistry in 1962.

[7] Edward Buchner, German biochemist, received the Nobel Award in chemistry in 1907.

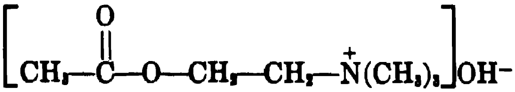
[8] James B. Sumner, American biochemist, together with J. H. Northrop and W. M. Stanley, received the Nobel Award in chemistry in 1946.

The synthesizing ability of living cells far surpasses that of chemists. For instance, a chemist could grind up a piece of meat, treat it with strong acids or caustic reagents, heat the residue in high-pressure chambers, whirl it in a centrifuge, extract it with delicate organic solvents at low temperatures in a multiple countercurrent extraction apparatus, vacuum distill the extracts, and chill the distillates in liquid air. Perhaps after several days, he might get a few crystals of a substance produced by our normal digestion. On the other hand, without resorting to any of these drastic conditions, we digest our food easily, quickly, and, fortunately, with pleasure. This is due to the miraculous catalytic action of enzymes. The average protein must be boiled for 24 hours in a solution of 20 per cent hydrochloric acid to be completely broken down. The body does the same thing in four hours or less, and without high temperatures and strong acids.

A single cell has an estimated 100,000 enzyme molecules. An enzyme molecule which splits hydrogen peroxide into water and oxygen—and creates the white foam when the antiseptic is placed on a wound—can transform more than 5 million peroxide molecules per minute.

Processes not involving oxygen carried on through enzyme activity are called *fermentations*. Generally, fermentation processes are limited by relatively high costs and the necessity of working in batches rather than continuous flow. Despite these disadvantages, fermentations are used industrially because of their specificity and production of optically active substances. For instance, the alkaloid ephedrine, which causes shrinkage of mucous membranes, can be synthesized, but a racemic mixture results. Only the *l*-form has the physiological activity; hence it is produced selectively with the aid of a suitable enzyme. Similarly, enzymes are employed in the production of several hormones, antibiotics, vitamins, citric and lactic acids, and certain alcohols. Enzymes are used also for other commercial processes. Some dry cleaners use enzymes to remove spots of egg, blood, beer, and coffee. An enzyme is used to remove pus and dead tissue in severe burns as an aid to medical treatment. An enzyme is used to clear wines, beer, and cider, which formerly became cloudy upon chilling. Then, of course, enzymes are used for the production of cheeses and alcoholic beverages.

b. Hormones and viruses (see also Chapter 28). Animal hormones may be defined as substances secreted by glands into the body fluids to control the operation of certain organs. Some hormones are ordinary low-molecular-weight substances such as acetylcholine, which depresses blood pressure.



$$\left[CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-O-CH_2-CH_2-\overset{+}{N}(CH_3)_3\right]OH^-$$

Acetylcholine

Several hormones, however, are proteins, such as insulin, oxytocin, and ACTH mentioned earlier.

At least 28 mammalian hormones have been identified. They form the most potent class of biologically active agents. For example, only 10^{-8} g is sufficient for glucagon, vasopressin, oxytocin or epinephrine to exert their effects—increase the blood pressure, release adrenal steroid, induce labor, etc. Hormones have a major role in medicine now, and the annual volume of sales in the United States amounts to several hundred million dollars.

A *virus* is an agent which will cause disease but is too small to be seen under a light microscope (photographs can be taken with an electron microscope) and cannot be filtered from solution with porcelain filters that hold back bacteria. It was presumed until 1935 that viruses were small microorganisms. In that year Nobel laureate Wendell Stanley crystallized a protein shown to cause the tobacco mosaic disease. In 1956, the virus that causes poliomyelitis was isolated in pure form. It is not known that all viruses are proteins, but those isolated so far have been proteins in combination with nucleic acids (high-molecular-weight organic acids containing heterocyclic nuclei).

Viruses have very high molecular weights (*ca.* 40 million) and have the ability to reproduce when placed in the proper animal or plant. They cannot live on sugars, meat broth, or other foods upon which bacteria thrive. Viruses are very specific about the type of cells in which they will reproduce. Cells of human beings are just right for the polio virus, but the cells of cats are not. However, cats contract other virus diseases that do not affect human beings. Ability to reproduce has long been taken as one criterion for life, so the question of whether or not viruses are living organisms has been debated. A recent view is that a virus is an enzyme capable of catalyzing its own formation.

c. Nucleic acids. In protein synthesis, cells use the random mixture of amino acids dissolved in the cellular fluid and the blood. The amino acids must be united in the specific order of the protein, and to do this there must be a specific process. This process is called the *template mechanism*, and nucleic acids are thought to be the templates. Templates are large molecules composed of thousands of constituent units called *nucleotides* linked by a phosphate ester bond (Figure 22.2).

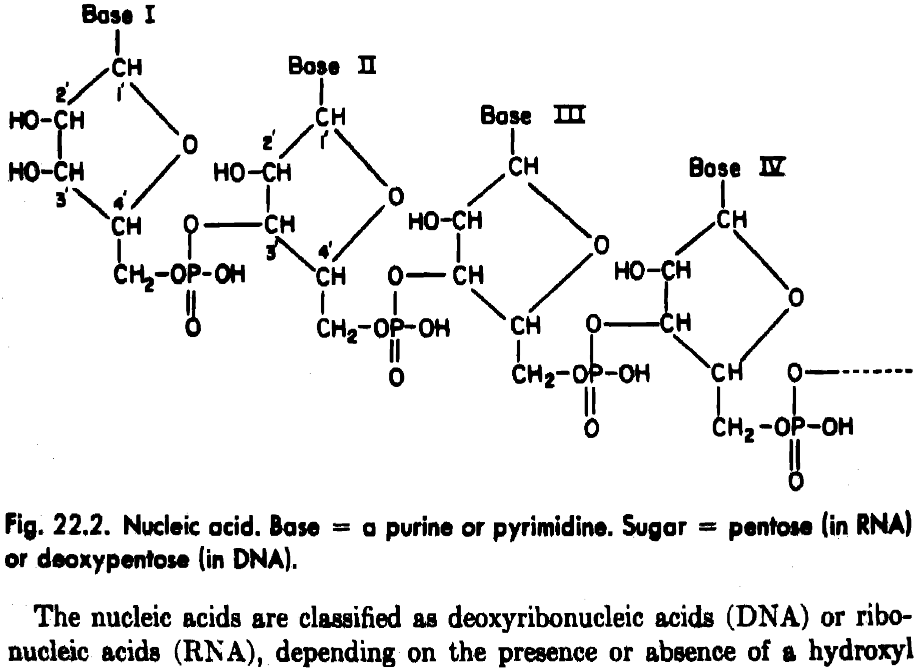
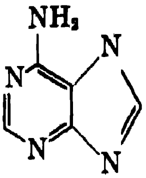
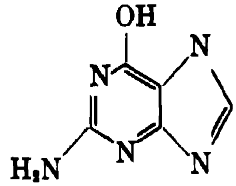
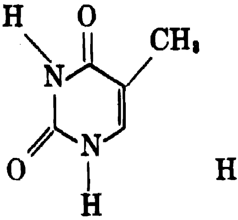
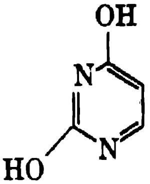
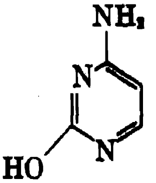


Fig. 22.2. Nucleic acid. Base = a purine or pyrimidine. Sugar = pentose (in RNA) or deoxypentose (in DNA).

The nucleic acids are classified as deoxyribonucleic acids (DNA) or ribonucleic acids (RNA), depending on the presence or absence of a hydroxyl group on the 2′ position of the pentose. DNA is found only in the chromosomes of the cell nucleus, whereas RNA is present in the nucleus and the cytoplasm.

Each nucleic acid contains four different kinds of nucleotide units, and the unit is distinguished by the type of base it contains.

During the past score years scientists have made amazing, penetrating probes of life and have placed several biological processes on a molecular basis. On the one hand they have shown how simple chemicals such as CO_2, H_2, NH_3, and CH_4 can be catalysed by ultraviolet radiation or an electric spark to form amino acids and simple polypeptides. Conceivably, these compounds could react further to yield proteins of greater and greater complexity until, finally, self-catalyzing substances were formed that could reproduce. On the other hand, scientists have recently explained genetics largely in terms of molecular processes.

Adenine Guanine
Purines

Thymine

Uracil Cytosine
Pyrimidines

All living tissue consists of cells which, when the cells are about to divide, are seen to contain circular regions surrounded by a thin membrane. Inside this membrane are bodies of various shapes that can be stained and are called *chromosomes*. In these chromosomes are linear, worm-like regions called *genes*, which have been shown to be the carriers of the cell's inheritance. Chemical analysis of chromosomes, from whatever organism, reveals that they contain the same two components, nucleic acids and protein. Hence, either the protein or the nucleic acids must be the carrier of inheritance. Experiments have shown it to be the nucleic acids alone which carry the genetic information.

Whereas genes consist of nucleic acids, all enzymes discovered to date are proteins (not all proteins are enzymes). It is believed that the function of the genes is to control the structural formation of proteins. If the nucleic acids are to convey genetic information, they must have a specific structure to form a chemical code. As stated above, nucleic acids consist of a long chain of repeating nucleotides characterized by the pattern of bases attached. In any one nucleic acid, these bases are of four different types. The fact that these bases are the only variable constituents of nucleic acids indicates that their sequence transmits a chemical genetic code written in a four-letter alphabet.

Thus, DNA and RNA serve as the templates for the synthesis of proteins (including enzymes). The situation has been likened to the procedure in making records. DNA is thought to be the master matrix, with RNA serving as a working mold. A master impression (DNA) serves to guide the cutting of thousands of similar records (RNA) which, in turn, are used to reproduce the musical patterns (proteins).

Nucleic acid replicates itself by this template mechanism each time a cell divides. If there is an aberration during replication and an incorrect base is incorporated into one of the daughter chains, then the genetic message is altered. The new genetic message may then be transmitted indefinitely from generation to generation, and this mutation will thereby give rise to a variety in the species. In this way, evolution could proceed in a series of small steps. The change in the amino acid sequence in a protein *would lead to the evolution of new enzymes which would catalyze different reactions* and lead to the development of new species, i.e., evolution.

Scientists of many countries have contributed to the present knowledge of DNA and RNA. For illustration, Dr. James Watson of Harvard and Dr. Francis Crick of Cambridge University worked out the spiral-ladder tertiary structure of DNA. Dr. Arthur Kornberg of Stanford and Dr. Servero Ochoa of New York University synthesized DNA and RNA, respectively, and received the 1959 Nobel Prize in medicine. Dr. Marshall Nirenberg of the National Institutes of Health first learned the code used by RNA and DNA in transmitting genetic information.

Research on nucleic acids is exciting because it appears that DNA and RNA may be involved in many complex life processes besides heredity, such as memory, aging, and virus diseases.

STUDY EXERCISES

1. Define or describe the following terms:

   (a) formol titration
   (b) zwitterion
   (c) polypeptide
   (d) a gene
   (e) an enzyme
   (f) a hormone
   (g) a virus
   (h) a protein
   (i) isoelectric point
   (j) a lactam

2. Describe a method of synthesizing a tetrapeptide from amino acids.
3. What is formed when a δ-amino acid is heated?

TEST QUESTIONS, Set 20

1. When 2.4 g of a protein, molecular weight 12,000, are treated with cold nitrous acid, then warmed up gently, 44.8 ml of N_2, STP, are produced. How many free primary amino groups per mole are there in the protein?

2. Why would glacial acetic acid rather than hexane be used as a solvent for the acetylation of amino acids with acetic anhydride?

3. A sample of tripeptide amino acid weighing 1.092 g reacted with nitrous acid to liberate 89.6 ml of N_2, STP.

   (a) Assuming one free NH_2 group and one acid group, what is the molecular weight of the tripeptide?
   (b) What volume of 0.5 N NaOH would be required to neutralize 5.46 g of the tripeptide?
   (c) If 1.37 g of the tripeptide were hydrolyzed in 50 ml of 1.0 N NaOH, what volume of 1.5 N HCl would be required to neutralize the excess alkali?

4. In a solution of pH 10, will glycine exist as an anion or as a cation?

23

Carbohydrates

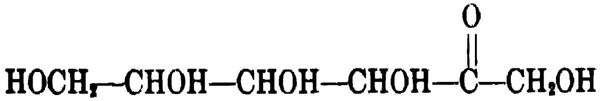
Carbohydrates include polyhydroxy aldehydes and ketones, and compounds convertible into these aldehydes and ketones by hydrolysis. Because the ratio of hydrogen to oxygen in these compounds is often 2 to 1, having the empirical formula $C_n(H_2O)_m$, they were given the term carbohydrate for "hydrate of carbon." The actual structures of carbohydrates, however, have no relationship to this notion. The simplest hydroxyaldehyde is glycolic aldehyde, $O{=}CH{-}CH_2OH$, which exhibits some of the properties of carbohydrates. Nevertheless, since carbohydrates are optically active substances, glyceraldehyde ($HOCH_2{-}CHOH{-}CHO$) is generally taken to be the "parent" carbohydrate.

23.1 CLASSIFICATION AND NOMENCLATURE

The class suffix for carbohydrates is *-ose.* One may have a triose, tetrose, pentose, hexose, etc., depending upon the number of carbon atoms forming a straight chain in the carbohydrate. Since the carbohydrate may be aldehydic (an aldose) or ketonic (a ketose), prefixes are used. Thus, an aldopentose is a 5-carbon atom aldehydic carbohydrate, and a ketohexose is a 6-carbon atom ketonic carbohydrate.

$$HOCH_2{-}CHOH{-}CHOH{-}CHOH{-}CHO$$

An aldopentose



$$HOCH_2{-}CHOH{-}CHOH{-}CHOH{-}\overset{\overset{\large O}{\|}}{C}{-}CH_2OH$$

A ketohexose

These simple carbohydrates are called *monosaccharides*, or *sugar units*, and are found in nature sometimes joined together through the loss of water molecules. Carbohydrates consisting of two sugar units are called *disaccharides*, those with three sugar units are *trisaccharides*, and those with many sugar units are *polysaccharides*. *Oligosaccharides* is a loose term referring to carbohydrates made up of from 2 to 10 sugar units. Because of stereoisomerism, there are 2 aldotrioses, 4 aldotetroses, 8 aldopentoses, 16 aldohexoses, etc., not to mention the ketoses. Each one of these carbohydrates which has been isolated has been given a separate name.

In general, although there are several exceptions, the monosaccharides and disaccharides are crystalline, water soluble, ether insoluble, somewhat sweet compounds, and are referred to as sugars. In contrast to this, the polysaccharides are usually amorphous, insoluble in water and in ether, and are tasteless; the most common are the starches and cellulose.

23.2 MONOSACCHARIDES

a. Structure determination. For experience, let us see how certain data could be used to determine the structure of a carbohydrate. An aldohexose will be used for illustration. The data are not presented in the order in which they might have been collected, but in a logical order, as they would be given in a report. The chemist would carry out many experiments, some fruitless and some informative, but he would select those for his report which lead most directly to his conclusion.

1. *Analysis and molecular weight determination indicate the unknown has a molecular formula of* $C_6H_{12}O_6$.

When working with a new compound, a chemist normally purifies it as much as he can, as indicated by its melting or boiling point, or any other appropriate physical property. He then analyzes it qualitatively for the elements, to learn which ones are present. Next, he makes quantitative analyses to ascertain its empirical formula. After measuring its molecular weight, its molecular formula can be determined.

2. *Reduction of the unknown with HI + phosphorus produces n-hexane.*

Normally, a chemist would next carry out various functional group analyses; i.e., he would make tests to ascertain which types of functional groups are in the unknown: aldehyde, acid, ester, etc. Among these tests might be the behavior toward different reducing agents, and in this case, HI + P was one. The fact that normal hexane is obtained reveals that the six carbon atoms form a straight chain.

3. *The unknown adds one mole of HCN.*

The unknown exhibits various carbonyl properties, such as reacting with hydroxylamine and phenylhydrazine, and since it adds only one mole of HCN, there must be either an aldehyde or a ketone group present, but not both.

4. *Oxidation of the unknown with bromine converts it into a monocarboxylic acid without loss of carbon atoms but with the loss of carbonyl properties.*

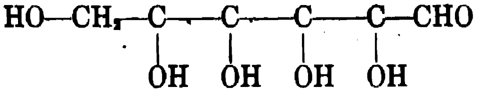
It will be found that several reactions and reagents used with carbohydrates are not commonly used with the other classes of compounds. Bromine and nitric acid used as oxidizing agents are two such reagents peculiar to carbohydrate chemistry. In this instance, the fact that a monocarboxylic acid is obtained without degradation indicates that either an aldehyde or primary alcohol group has undergone oxidation. Recall that ketones and secondary and tertiary alcohols give carboxylic acids only with degradation. In this case, since the acid that arises no longer has carbonyl properties, it must have been the carbonyl group that was converted into the acid group. This means the carbonyl group was an aldehyde group. So far, this gives C—C—C—C—C—CHO for the structure of the unknown. The aldehyde group must be at the end of the chain to have a straight chain of carbon atoms.

5. *Oxidation of the above monocarboxylic acid with nitric acid yields a dicarboxylic acid without the loss of carbon atoms.*

Since the monocarboxylic acid has no carbonyl group, the only other type of group which will give rise to a carboxyl group without degradation is a primary alcohol group. Hence, there is a primary alcohol group in the monocarboxylic acid and, therefore, in the unknown. This gives us for its structure so far, CH_2OH—C—C—C—C—CHO.

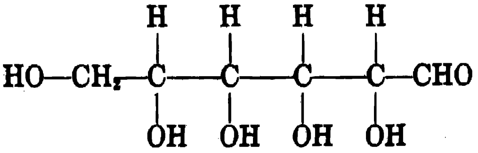
6. *Reaction with acetic anhydride liberates five equivalents of acid.*

As discussed in Section A-46 (Appendix), the liberation of five equivalents of acid indicates the presence here of five OH groups. Since two OH's on the same carbon atom is an unstable structure, and the unknown is a normally stable compound, the five OH's will be placed on five different carbon atoms. One is already found to be a primary alcohol, and the other four will be placed on the four available center carbon atoms.



$$\mathrm{HO{-}CH_2{-}\underset{OH}{\underset{|}{C}}{-}\underset{OH}{\underset{|}{C}}{-}\underset{OH}{\underset{|}{C}}{-}\underset{OH}{\underset{|}{C}}{-}CHO}$$

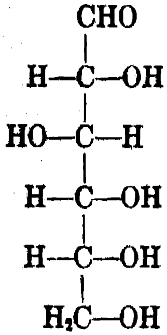
This accounts for the six C's, six O's, and eight of the 12 H's of the molecular formula $C_6H_{12}O_6$. To take care of the four remaining H's and to conform with valence rules, the four H's should be placed on the four center carbon atoms.



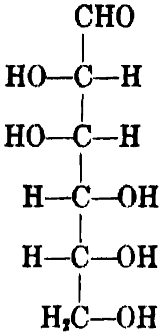
$$\mathrm{HO{-}CH_2{-}\overset{H}{\overset{|}{\underset{OH}{\underset{|}{C}}}}{-}\overset{H}{\overset{|}{\underset{OH}{\underset{|}{C}}}}{-}\overset{H}{\overset{|}{\underset{OH}{\underset{|}{C}}}}{-}\overset{H}{\overset{|}{\underset{OH}{\underset{|}{C}}}}{-}CHO}$$

In this fashion, one might have worked out the structure of the hexose, although the relative orientations of the four OH's about the four center carbon atoms are still unknown.

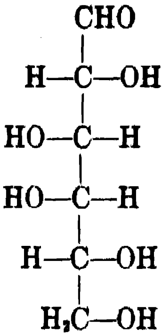
b. Reactions of monosaccharides. Since hexoses are the most common monosaccharides, they will be used for illustration. The configurational structures of four of the most common hexoses—glucose, mannose, galactose, and fructose—are given below.



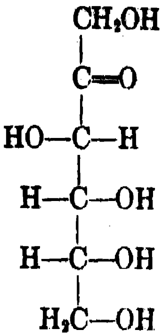
Glucose
Found in fruits, blood, and urine. From sugar cane and starch by hydrolysis.



Mannose
From plants by hydrolysis.



Galactose
From milk sugar by hydrolysis.

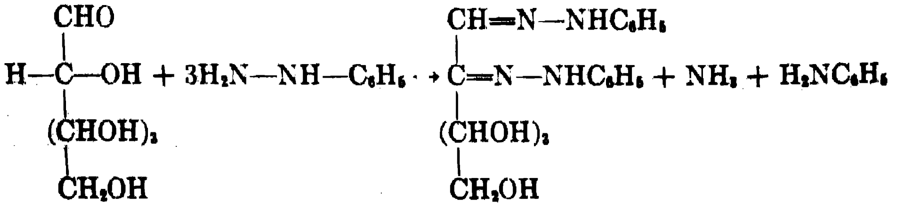


Fructose
Found in fruits and honey. From sugar cane by hydrolysis.

Given under 13 headings on the following pages are certain important reactions of monosaccharides.

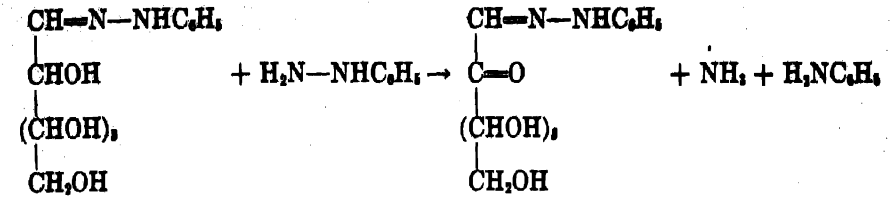
1. Molisch test: When a carbohydrate is dissolved or suspended in water in a test tube with a phenolic substance (page 498), and then conc. H_2SO_4 is carefully poured down the side of the tube to form two layers, a deep red to violet color is formed at the interface of the two liquid layers. This test is used for the qualitative detection of carbohydrates in general and is known as the Molisch test.

2. Phenylosazone formation:



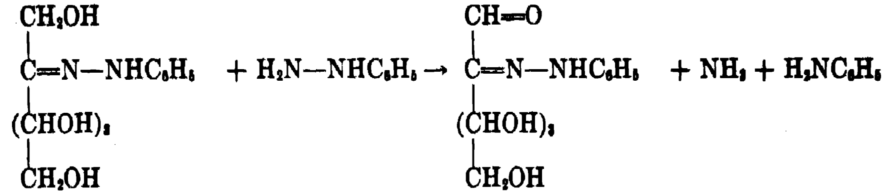
$$\begin{array}{l} CHO \\ | \\ H-C-OH \\ | \\ (CHOH)_3 \\ | \\ CH_2OH \end{array} + 3H_2N-NH-C_6H_5 \rightarrow \begin{array}{l} CH=N-NHC_6H_5 \\ | \\ C=N-NHC_6H_5 \\ | \\ (CHOH)_3 \\ | \\ CH_2OH \end{array} + NH_3 + H_2NC_6H_5$$

The first mole of phenylhydrazine reacts with the monosaccharide just as it would with any carbonyl compound, forming a phenylhydrazone. Because of the water-solubilizing effect of the several OH groups through hydrogen bonding with water molecules, most phenylhydrazones of sugars are hard to isolate. A second mole of phenylhydrazine effectively oxidizes the α-alcohol group to a keto group.



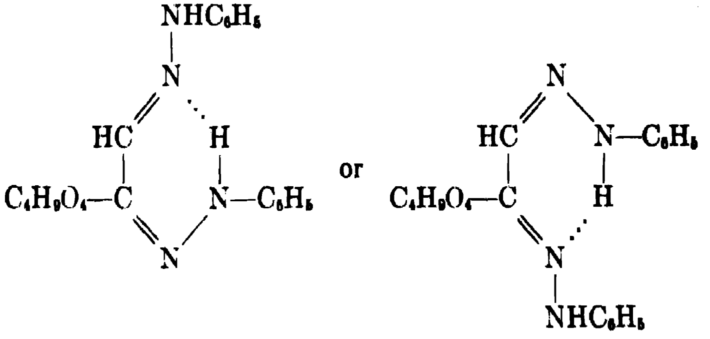
$$\begin{array}{l} CH{=}N{-}NHC_6H_5 \\ | \\ CHOH \\ | \\ (CHOH)_3 \\ | \\ CH_2OH \end{array} + H_2N{-}NHC_6H_5 \rightarrow \begin{array}{l} CH{=}N{-}NHC_6H_5 \\ | \\ C{=}O \\ | \\ (CHOH)_3 \\ | \\ CH_2OH \end{array} + NH_3 + H_2NC_6H_5$$

or, for a ketose phenylhydrazone,



$$\begin{array}{l} CH_2OH \\ | \\ C{=}N{-}NHC_6H_5 \\ | \\ (CHOH)_3 \\ | \\ CH_2OH \end{array} + H_2N{-}NHC_6H_5 \rightarrow \begin{array}{l} CH{=}O \\ | \\ C{=}N{-}NHC_6H_5 \\ | \\ (CHOH)_3 \\ | \\ CH_2OH \end{array} + NH_3 + H_2NC_6H_5$$

Then, the third mole of phenylhydrazine reacts with the new carbonyl group to form the phenylosazone. One immediately asks, Why does the reaction stop after the introduction of two phenylhydrazine residues? Evidence has been found to show that the phenylosazone is stabilized by chelation.



It thereby resists further reaction with the phenylhydrazine. Phenylosazones are yellow to orange-red crystalline compounds sometimes used as derivatives for the identification of carbohydrates.

The structures of phenylosazones will be the same for the first two carbon atoms. Since glucose and mannose have identical structures below the C_2 carbon atoms, they give rise to the same phenylosazone.[1] This is true also for fructose, even though fructose is a ketose, for it has the same structure as glucose and mannose below the C_2 carbon atom. This means that these three sugars could not be differentiated on the basis of the melting points of the phenylosazone obtained from each. On the other hand, galactose differs from glucose with respect to the orientation of the H and OH about the

---

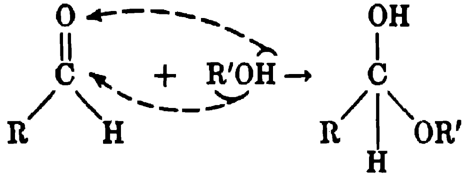
[1] Mannose is unusual in that it gives a colorless phenylhydrazone which is slightly soluble in hot water. However, continued heating with excess phenylhydrazine slowly converts the phenylhydrazone to mannose phenylosazone, which is identical to glucose phenylosazone.

C_4 carbon atom. Galactose would, therefore, give a different phenylosazone from that of glucose.

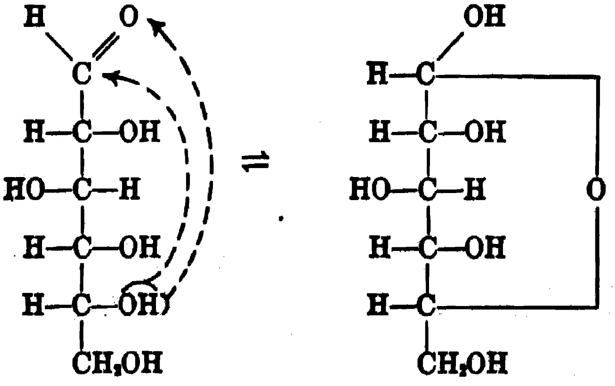
3. *Oxidation:* Those carbohydrates having free carbonyl groups reduce Fehling's and Tollens' reagents just as ordinary aldehydes do. Although these reagents normally are reduced only by aldehydes, α-hydroxyketones are also oxidized. Hence, ketoses give positive tests toward these two reagents. There are some carbohydrates, however, whose carbonyl groups are tied up (this will be shown presently), and these do not reduce Tollens' or Fehling's reagents. They are referred to as nonreducing sugars.

4. *Hemiacetal formation and mutarotation:* If a sample of glucose were recrystallized from water, it would be found that a freshly prepared aqueous solution of this sample would have a specific rotation of +113°, and upon standing, this value would steadily change to +52° and remain there. On the other hand, if a sample of the same glucose were recrystallized from pyridine, a freshly prepared aqueous solution would have a specific rotation of +19°, which would steadily increase upon standing and level off at a constant value of +52°. This changing of optical rotation with time is referred to as *mutarotation*. The fact that the two portions of glucose when recrystallized from different solvents mutarotate and stop at the same position, suggests the formation of some equilibrium mixture.

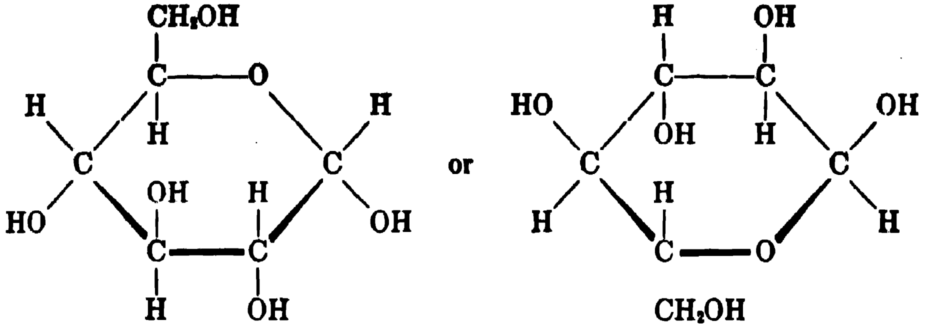
It was shown on page 320 that an alcohol may add to an aldehyde to yield a hemiacetal:



Now, sugars contain an aldehyde or keto group and several alcohol groups within the same molecule, and one might wonder if the answer to the mutarotation of glucose lies in an intramolecular hemiacetal formation.

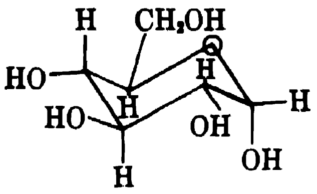


The OH from the δ-carbon atom (C_5) is used here, and evidence for choosing this carbon atom will be given presently. The hemiacetal has a normal cyclic structure and may be drawn as such, which is called a *Haworth structure*.[3]



Haworth structures of α-D-glucose

The various groups attached to the carbon chain are drawn up or down to indicate their spatial orientation. When the ring-oxygen atom is drawn in the upper right-hand corner of the ring, OH groups below the ring correspond to the right side in the vertical structure. When the ring-oxygen atom is drawn in the lower right-hand corner of the ring, OH groups extending upward would appear on the right side of the vertical structure. These Haworth structures more closely resemble the actual structures, but often the vertical structural formulas are used for convenience. It may be due to habit, but it seems that the relative positions of the OH groups are more quickly recognized from the vertical structures.



Even more meaningful are the conformational structures which reveal the axial or equatorial projections of the substituents. It can be seen, for example, that all of the substituents are equatorial in β-D-glucose and all but the OH on C_1 are equatorial in the α anomer.

When the alcohol group is added to the carbonyl group in hemiacetal formation, either one of the bonds of the C═O group may break. This will cause the arising OH group to swing out to the right or left (up or down in Haworth structures). This accounts for the crystalline glucoses having different initial specific rotations. A configuration in which the OH on the C_1 carbon atom is on the same side as the ring oxygen in the vertical structural formula is called α. The opposite configuration is called β. The α and β modifications of a particular sugar, of the same ring size, differ in configuration only at the hemiacetal positions and are called *anomers*. In solution, the two anomers may reversibly form the same aldehyde, and, once the aldehyde is formed, either anomer may

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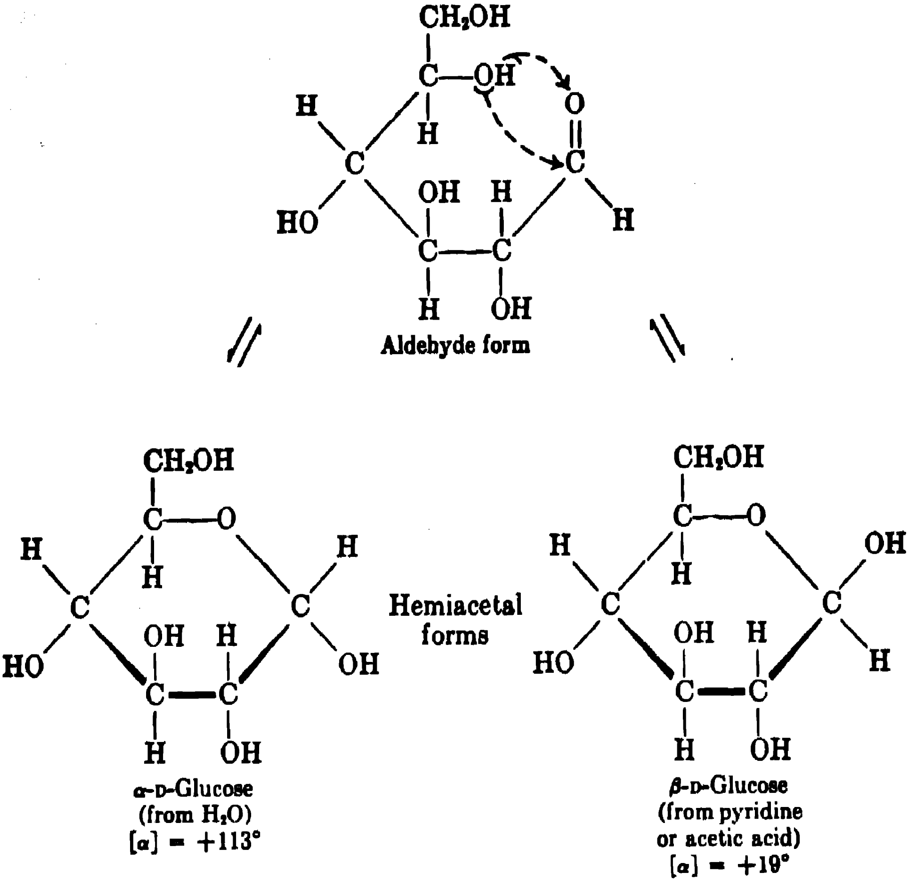
[3] W. N. Haworth, British chemist, together with P. Karrer, received the Nobel Award in chemistry in 1937.

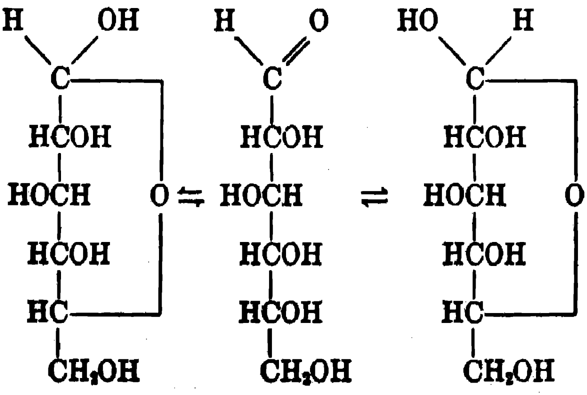


Aldehyde form

Hemiacetal forms

α-D-Glucose (from H_2O) [α] = +113°

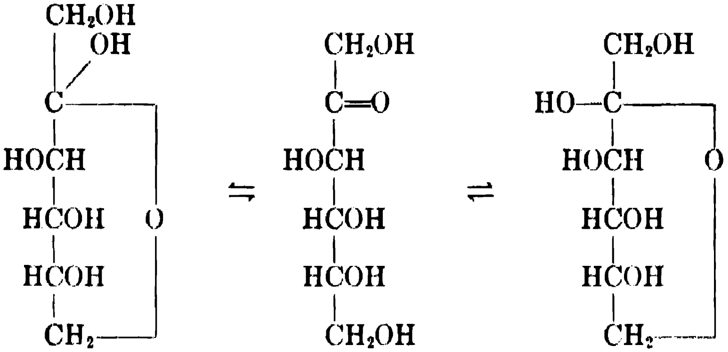
β-D-Glucose (from pyridine or acetic acid) [α] = +19°



α-D-Glucose D-Glucose β-D-Glucose

be formed from the aldehyde. Hence, when either anomer is placed in solution, a portion changes to the aldehyde, which may then form some of the other anomer. This reversible reaction continues until the equilibrium mixture results. The same equilibrium mixture is obtained by starting with either anomer. The amount of the sugar in the aldehyde form in the equilibrium mixture is very small, usually five per cent or less. However, since there is an equilibrium, any reaction which uses up the aldehyde form causes the equilibrium to shift to yield more aldehyde, and thereby, the entire material may react as if it were all present as an aldehyde. For example, phenylosazones are formed by reactions of the carbonyl form of sugars, and all of the sugar present reacts as if it had this structure only. On the other hand, acetal formation (next reaction) is with the hemiacetal form, and all of the sugar present reacts as if it had this structure only.

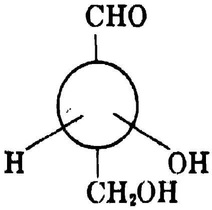
This hemiacetal formation and mutarotation occurs with virtually all ketoses and aldoses whose carbonyl groups are not tied up in another way (as shown in reaction 5). For example, one can write for fructose:



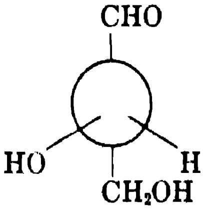
α-D-Fructose D-Fructose β-D-Fructose

As a general rule, monosaccharides give hemiacetals involving six-membered rings, called *pyranose rings*. A sugar having a five-membered ring is called a *furanose*. These are usually unstable and tend to isomerize to the pyranose. In reaction 11 it is shown how the size of the ring may be determined.

Glyceraldehyde has one asymmetric carbon atom and, therefore, may exist in two forms, a *dextro* and a *levo* form.



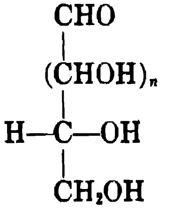
D-Glyceraldehyde



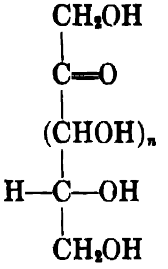
L-Glyceraldehyde

Just which is the structure of the *dextro* isomer could not be shown fifty years ago, and Emil Fischer arbitrarily chose the *dextro* isomer to be the one with the

OH written on the right when the H and OH extend forward toward the observer. As mentioned previously, not until about ten years ago was it possible to determine the absolute stereo structure of optical isomers (cf. page 454), and it was found that, indeed, the model Fischer chose for the D-glyceraldehyde is really that of the dextrorotatory isomer. Nevertheless, Fischer's suggestion, later modified by Rosanoff and translated into ring structures by Haworth, was accepted generally, and all sugars having the OH group on the right of the carbon above the primary alcohol group are conventionally designated as D isomers, irrespective of whether they are dextrorotatory or levorotatory.

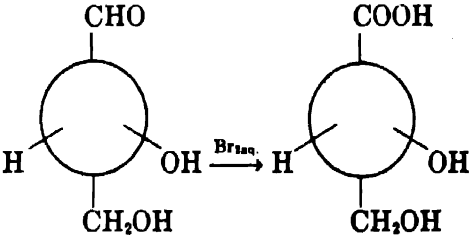


D-Aldoses



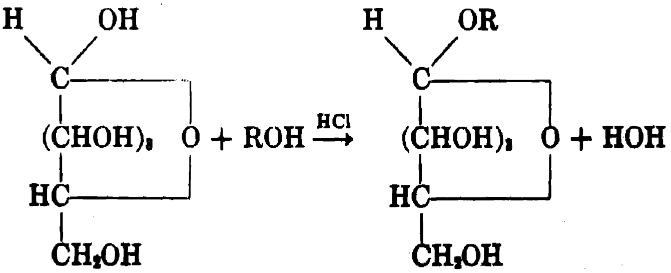
D-Ketoses

Hence, glucose is designated D-glucose. The natural isomer is actually dextrorotatory. Fructose, too, is designated D, but the natural isomer happens to be levorotatory. This is indicated by placing a minus sign in parentheses, such as D(−)-fructose. Similarly, the acid obtained from the oxidation of D(+)-glyceraldehyde is levorotatory and called D(−)-glyceric acid.



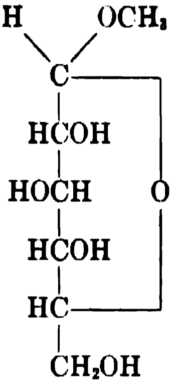
D(+)-Glyceraldehyde D(−)-Glyceric acid

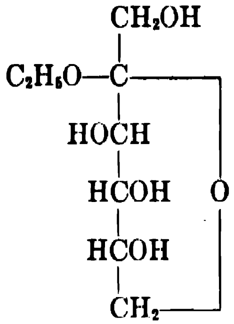
5. *Acetal formation:* The hemiacetal form of sugars may be converted into full acetals by treatment with an alcohol and hydrogen chloride.



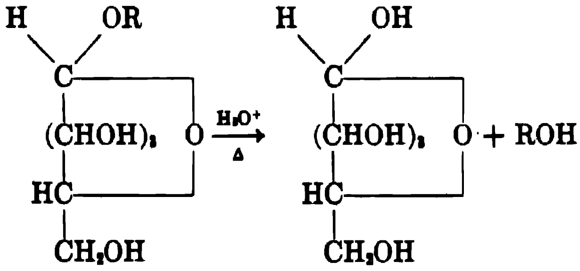
An acetal

The reaction is more conveniently catalyzed by using an ion exchange resin in its acid form. The product is an acetal—a compound having two OR groups attached to a single carbon atom—although, in this case, one R group is also joined to the acetal carbon atom through a carbon chain. These acetals are regarded as alkyl oside derivatives of the respective sugars, and their names are based on those of the alkyl group and the sugar. Hence, for R = methyl, and with glucose, the acetal is called methyl glucoside.

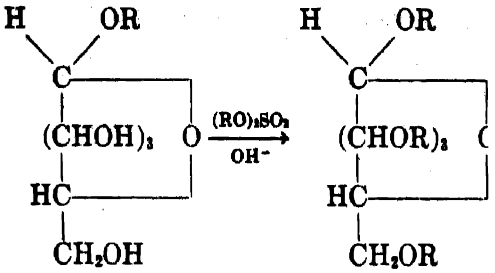

α-Methyl-D-glucoside


β-Ethyl-D-fructoside

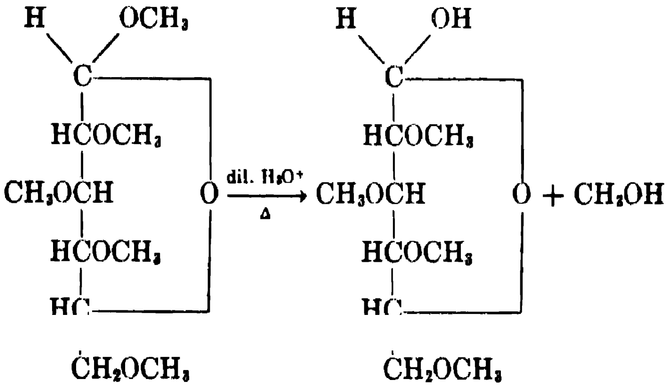
Alkyl groups cannot migrate back and forth between the oxygens on the C_1 and C_5 carbon atoms as the hydrogen atom does with the sugars. Therefore, the acetal does not contain a potential carbonyl group. Accordingly, it does not reduce Tollens' or Fehling's reagents or form a phenylosazone. The acetals are readily hydrolyzed in dilute acid. And the products, of course, will then reduce Tollens' and Fehling's reagents:



6. *Polyalkylation and polyacylation:* Alkylation with alcoholic hydrogen chloride alkylates only the C_1 hydroxyl group. The remaining OH groups may be alkylated upon treatment with alkyl sulfate in aqueous alkali or silver oxide plus methyl iodide in dimethylformamide. In most instances the R will be methyl or ethyl, because the major use of this step is to replace the active hydroxylic hydrogen atoms by some alkyl group without regard to which simple alkyl group is used. However, all of the C—OR bonds are ether



linkages, except those at the C_1 atom, the latter being an acetal structure. It will be recalled that acetals hydrolyze quickly in dilute acid, but ethers hydrolyze slowly and only in concentrated acids. Hence, it is easy to remove selectively the top alkyl group.

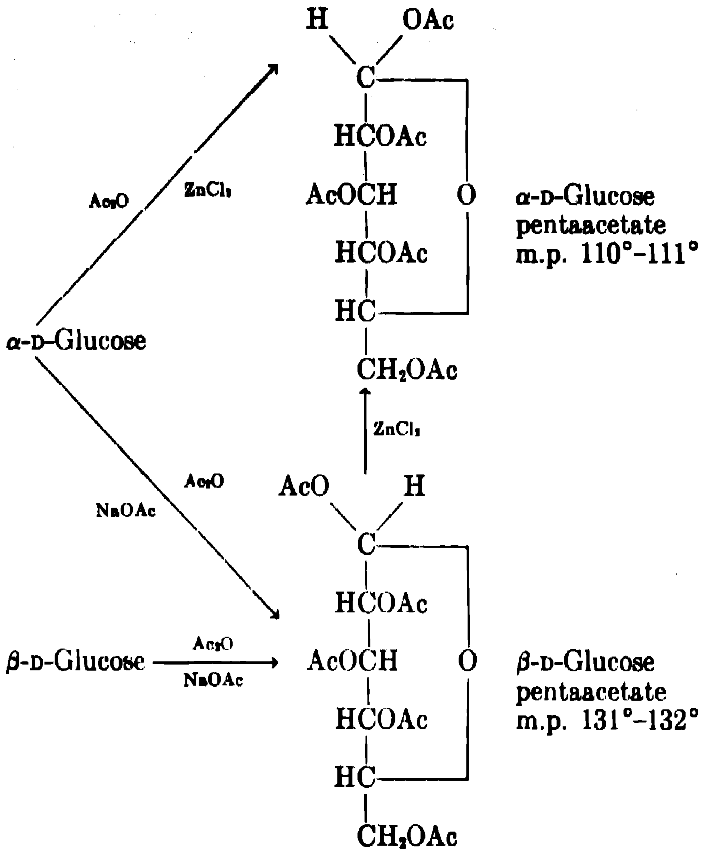


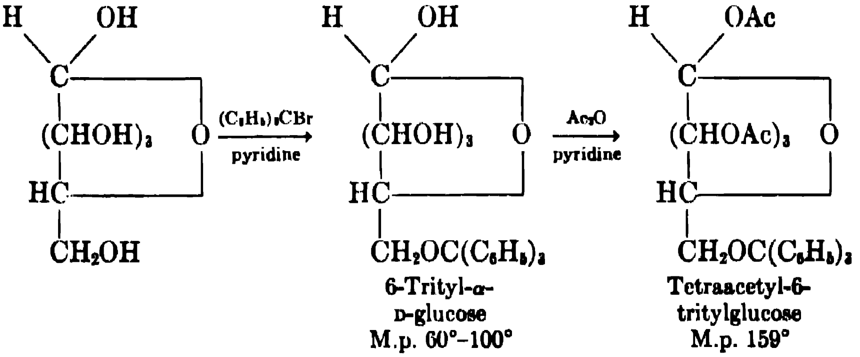
Tetramethyl-α-methylglucoside Tetramethylglucose

The tetramethylglucose may isomerize to the aldehyde form and mutarotate. It will also reduce Tollens' and Fehling's reagents.

Hydroxylic hydrogen atoms may also be replaced by acyl groups in the usual manner through the use of acid chlorides or acid anhydrides. As with the acetals, α and β acetates may be obtained. For example, glucose gives rise to two pentaacetates (page 543). This is another example of kinetic control vs. thermodynamic control of reactions. With an acid catalyst, the α and β anomeric acetates equilibrate, and the more stable α form is the major product. In a basic medium the esters do not equilibrate, so that the faster-forming β isomer predominates in the product mixture.

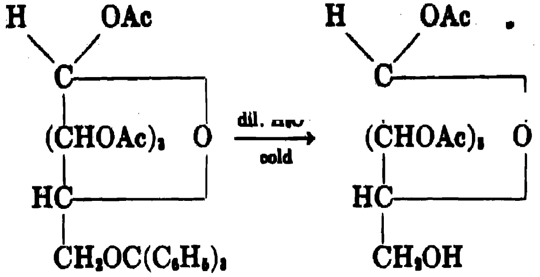
On some occasions, the polyacyl products may serve as derivatives, but sometimes the reaction product is a mixture, and therefore is unsuitable. A good derivative is a combination acetyl-trityl sugar product. Triphenylmethyl bromide, $(C_6H_5)_3C—Br$, commonly called trityl bromide, reacts with primary alcohols in preference to secondary alcohols. The sugar may be tritylated in pyridine solution, then acetylated in the same solution.





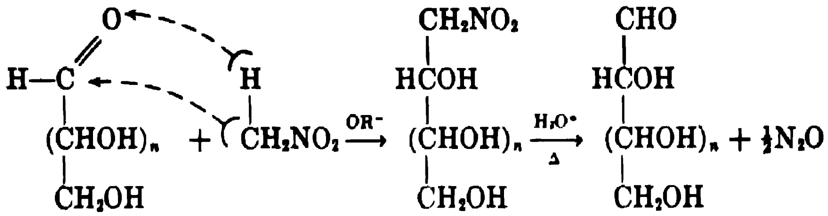
The trityl sugars often are not sharp-melting, but the acetylation products are. Trityl ethers hydrolyze very easily in acid media, so the 6-trityl group may be hydrolyzed off selectively (page 544).

It can be seen then, that it is possible to alkylate (1) only the C_1—OH group, (2) all but the C_1—OH group, (3) only the primary OH group, or (4) all OH groups. Also, one may acylate all OH groups, or all but the primary alcohol group.



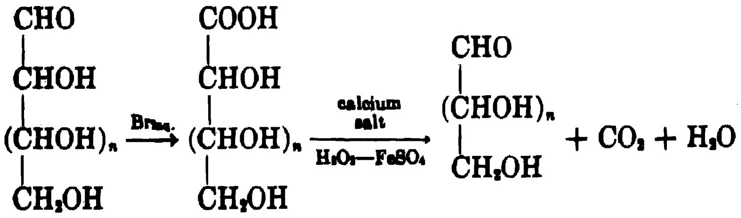
1,2,3,4-Tetraacetylglucose

7. Chain degradation and chain lengthening: The carbon chain of monosaccharides may be shortened or lengthened by one carbon atom at a time. The carbon chain may be increased by several methods involving the use of HCN, nitromethane, diazomethane, or Grignard reagents. One of the early-developed and long-used methods is that of Kiliani, called *Kiliani's cyanohydrin synthesis*. It uses HCN to form a cyanohydrin, and the CN group is converted into a formyl group through a series of reactions. A simpler method is one that uses nitromethane:



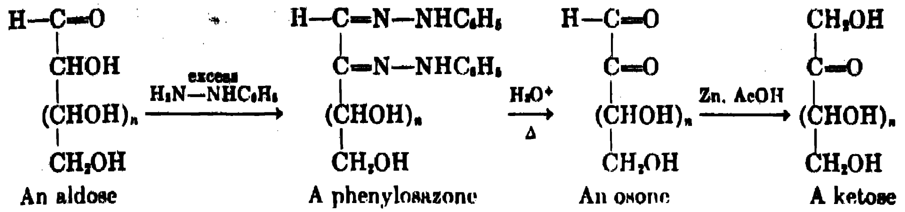
This is really an application of the Nef reaction given on page 431.

Several methods have been used for the degradation of sugars. A simple one is that of Ruff:



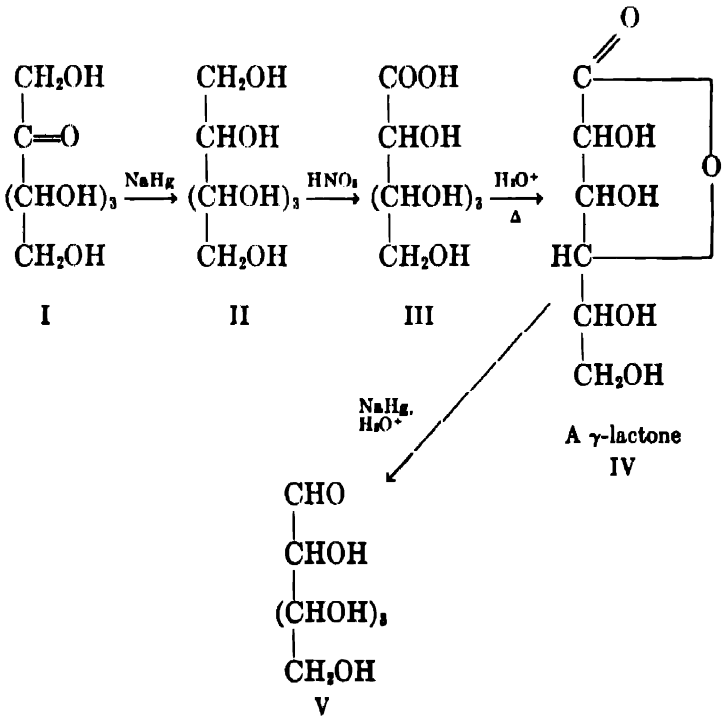
The ferrous sulfate-hydrogen peroxide mixture is known as *Fenton's reagent*.

8. Aldose to ketose to aldose: Aldoses and ketoses are interconvertible through a sequence of reactions. To transform an aldose to a ketose, one makes use of the phenylosazone:



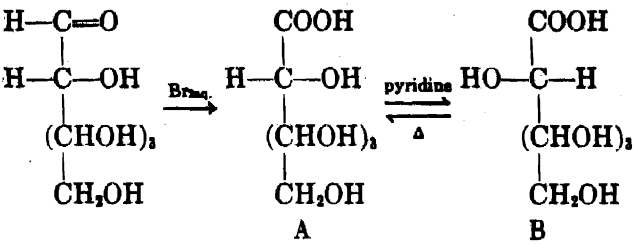
In glacial acetic acid, zinc reduces the aldehyde group in preference to the ketone group.

The transformation of a ketose to an aldose is a longer process:



Either primary alcohol group of II may be oxidized, giving rise to two different acids, and they have to be separated by fractional crystallization. When the hydroxy acid III is heated in an acid medium, it undergoes lactone formation, and generally the OH from the γ-carbon atom is involved. Upon reduction of the lactone in dilute mineral acid, the corresponding aldose V is produced. Failure to use an acid medium here carries the reduction down to the alcohol II.

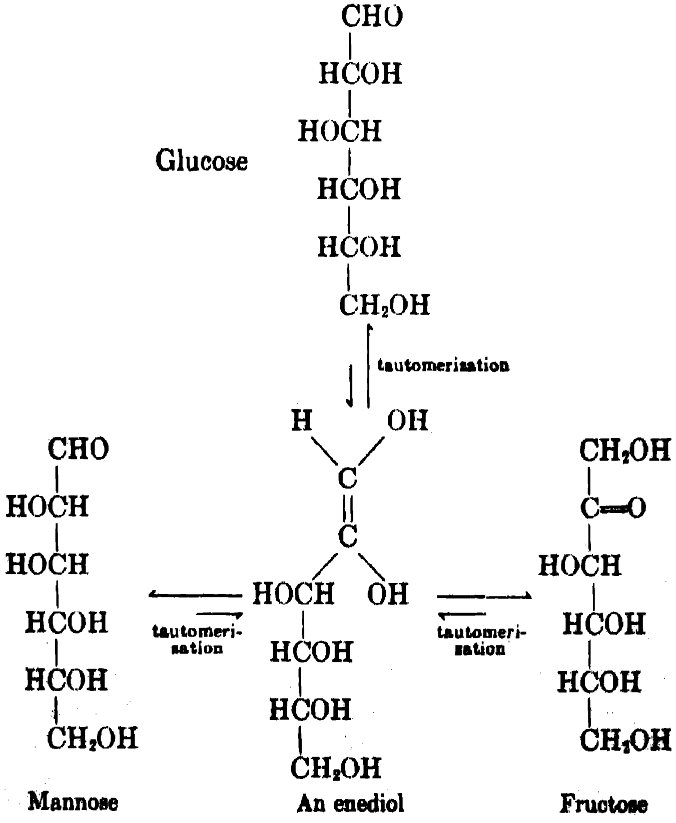
9. *Epimerization:* Epimers are sugars which differ only in the orientation of the OH group at the α-carbon atom. Hence, glucose and mannose are epimers. Epimers are just a special class of isomers. The process of going from one epimer to another is called *epimerization.*



When the hydroxy acids A or B are heated in pyridine, an equilibrium mixture of the two is produced. They are separated by fractional crystallization, and the desired isomer, in this case B, is converted to a lactone and reduced with sodium amalgam to the aldose, as was done in the preceding reaction.

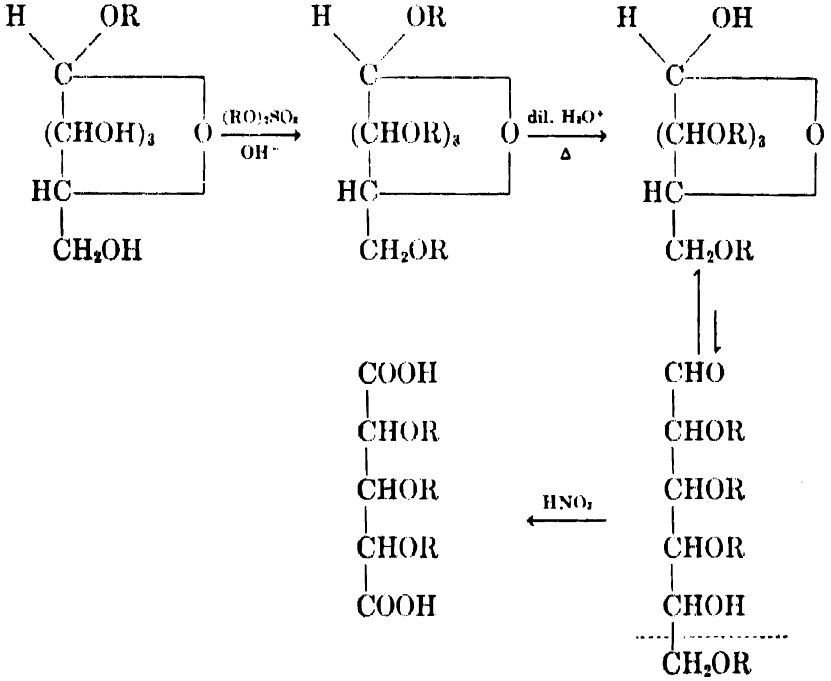
In the last three reactions it has been shown how to decrease or increase a sugar carbon chain, how to isomerize the α-OH group, and how to interconvert aldoses and ketoses. Note that in order to increase or decrease the carbon chain of a ketose, it must first be transformed to an aldose, the chain lengthened or shortened, then the resulting aldose changed to the ketose.

10. Action of alkali on aldoses: Aqueous alkali produces two types of reactions with aldoses, depending upon the alkalinity of solution. Dilute alkali at room temperature catalyzes a slow isomerization, known as the *Lobry de Bruyn*



and van Ekenstein transformation after its discoverers. For example, if glucose is allowed to stand for several days with dilute calcium hydroxide, there results a mixture of glucose, mannose, and the corresponding ketose, fructose. The reaction is reversible, and a mixture of the three sugars is produced, starting with any one of the three. Concentrated alkali brings about a degradation of monosaccharides, producing formaldehyde, hydroxyacetaldehyde, and a mixture of degraded sugars. Furthermore, some isomerization may occur and also the aldehydes may undergo condensations. Consequently, many products are formed, and the exact course of the reaction is too complex for description here.

11. Ring-size determination: Up to here, use has been made of the general rule that hemiacetal forms of sugars involve the δ-OH group and sugar lactones involve γ-OH groups. These rules can be confirmed as follows. The sugar is completely alkylated; then the oside alkyl group is hydrolyzed off to give a tetraalkyl hexose. The latter is then oxidized with nitric acid.

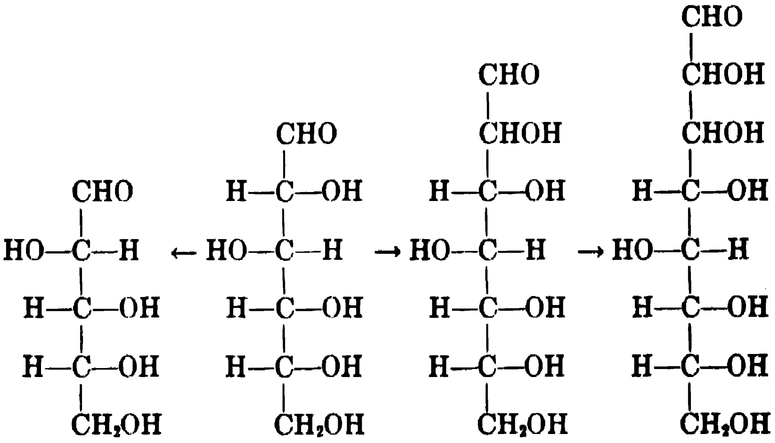


The product is a five-carbon chain dicarboxylic acid, which fact has to be verified by a structure determination. In the oxidation, the aldehyde and secondary alcohol groups suffer oxidation, but the ether carbon atoms are unaffected. This is to be expected, since ethers and saturated hydrocarbons are usually resistant to oxidation. The recovery of a five-carbon chain dicarboxylic acid (in addition to some four-carbon acid) indicates that the C_5 carbon atom of the tetraalkyl hexose was unprotected from oxidation.

This was so because, during the alkylation process, it was tied up by ring formation. In this way, then, one may find out which OH is involved in ring formation in the hemiacetal form of a sugar.

12. Hydroxyl group orientations: Another structural feature of monosaccharides to be determined is the orientation of OH groups along the carbon chain. This can be done on the basis of an empirical rule developed by C. S. Hudson. By studying various sugars, Hudson found that if the γ-OH group of a sugar is on the left when the sugar is oxidized to its respective acid and converted to the γ-lactone, the lactone will be levorotatory. If the γ-OH of the sugar is on the right side of the chain, the corresponding lactone will be dextrorotatory. Hence, glucose gives a dextrorotatory lactone and galactose gives a levorotatory lactone.

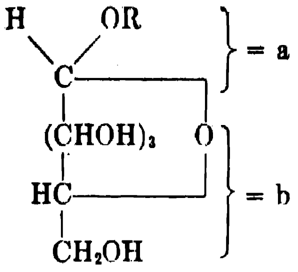
To determine the orientation of the other OH groups, the carbon chain is lengthened or shortened by one carbon at a time, and then the respective lactones are produced. For illustration, if glucose is converted to a heptose, the γ-OH group of the heptose is the former β-OH group of glucose. Determination of the orientation of the γ-OH group in the heptose, then, reveals the orientation of the former β-OH group of glucose.



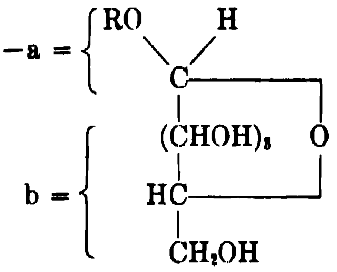
A pentose Glucose A heptose An octose

Upon conversion of the heptose to an octose, the former α-OH group of glucose becomes the γ-OH group of the octose. Its orientation may be ascertained in the same fashion; hence, the orientations of the OH groups about the C_2, C_3, and C_4 carbon atoms of glucose have been determined. To learn the orientation about the C_5 atom, one degrades the glucose by one carbon atom. Now, the γ-carbon atom of the pentose is the former δ-carbon atom of glucose. Upon determining the orientation of the γ-OH of the pentose, one learns the orientation of the δ-OH group of glucose.

In 1898 van't Hoff proposed a method of determining the contribution of specific carbon atoms to the total optical activity of a sugar. For illustration, take two anomers:



An α-hexoside
[α] = R



A β-hexoside
[α] = S

The structures below the C_1 atoms are identical, and therefore make the same contribution to the measured optical activities, R and S. The structures about the C_1 atoms are mirror images of one another, and have equal but opposite effects upon the total optical activities. The observed optical activity R of one isomer is equal to the sum of the contributions a and b, while S is equal to $(-a + b)$.

$$R = a + b \qquad S = -a + b$$

Remember that R and S are experimentally determined quantities. The values R and S may be added, and when substitutions are made, the sum is found to equal $2b$ algebraically.

$$R + S = (a + b) + (-a + b) = 2b.$$

The difference is $2a$ or $-2a$, depending upon which is subtracted from the other.

$$R - S = (a + b) - (-a + b) = 2a$$

$$S - R = (-a + b) - (a + b) = -2a$$

All that is sought is the magnitude, so that a knowledge of $2a$ or $-2a$ will serve. Half the sum of R and S gives the contribution of the body of the sugar to its total optical activity, and half the difference gives the contribution of the C_1 atom. For example, the optical rotations of the methyl-D-glucosides and the methyl-D-fructosides are as follows:

	$[\alpha]_D$	$[M]_D$
Methyl α-D-glucoside	+157.9°	+30,600
Methyl β-D-glucoside	−32.5°	−6,300
Methyl α-D-fructoside	+93°	+18,100
Methyl β-D-fructoside	−47°	−9,130

The sum of the molecular rotations of the methyl glucosides divided by twice the molecular weight of methyl glucoside gives the contribution of the body of the sugar toward the observed specific rotations.

$$\begin{array}{r} +30{,}600 \\ -\ 6{,}300 \\ \hline +24{,}300 \end{array} \qquad \frac{+24{,}300}{2 \times 194} = +62.7^\circ$$

The effect of the C_1 carbons on the observed specific rotations is obtained from the difference of molecular rotations.

$$\begin{array}{r} +30{,}600 \\ -(-6{,}300) \\ \hline +36{,}900 \end{array} \qquad \frac{+36{,}900}{2 \times 194} = +95.2^\circ$$

Similar computations for α- and β-D-glucose would show the contributions of the C_1 carbon atoms in these sugars. Such comparisons of α-D-glucose with α-D-mannose, and of α-D-glucose with α-D-galactose will give the contributions of the C_2 and C_4 atoms, respectively.

13. Glycosides: Many acetals, comparable to the methyl glucosides, are found in nature, being derived from combinations of various hydroxy compounds with various sugars. As a class, these compounds are called *glycosides.* They may be hydrolyzed by mineral acids or enzymes. Fischer first noted that an enzyme, maltase, will hydrolyze only α-glucosides, and a different enzyme, emulsin, will hydrolyze only β-glucosides. Since then, this specificity of these two enzymes has been found to be generally true and is frequently used as a method of determining the α- or β-configurations of glycoside linkages.

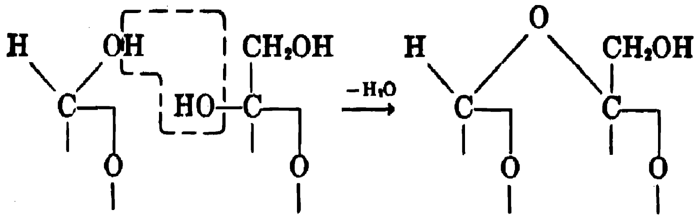
23.3 DISACCHARIDES

When the acetal group of a glycoside is a monosaccharide sugar, the glycoside is a disaccharide. Three common glycosides of this type will be discussed to illustrate the general properties of disaccharides.

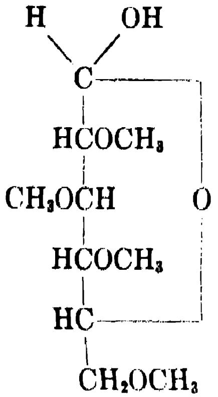
a. Sucrose. Sucrose is the common table sugar obtained from sugar cane. It has an empirical formula $C_{12}H_{22}O_{11}$. It does not form a phenylosazone or exhibit carbonyl properties. Upon hydrolysis in dilute acid, it yields glucose plus fructose.

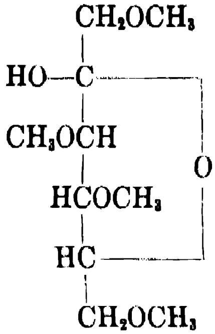
$$\underset{\text{Sucrose}}{C_{12}H_{22}O_{11}} + H_2O \xrightarrow[\Delta]{H_3O^+} \underset{\text{Glucose}}{C_6H_{12}O_6} + \underset{\text{Fructose}}{C_6H_{12}O_6}$$

The structure of sucrose is easily deduced from a few facts. (1) Hydrolysis of sucrose yields glucose and fructose. Hence, the basic sugar units are known and one merely needs to find how the sugar units are joined. (2) Sucrose is a nonreducing sugar. Hence, there are no potential carbonyl groups, and the two sugar units must be linked together at the oside carbon atoms.

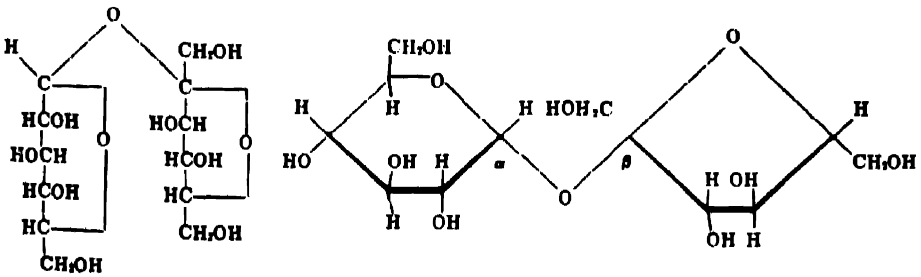


(3) Complete methylation of sucrose, followed by mild hydrolysis, yields 2,3,4,6-tetramethylglucose and 1,3,4,6-tetramethylfructose.


2,3,4,6-Tetramethylglucose


1,3,4,6-Tetramethylfructose

Only the acetal bonds have been hydrolyzed. From the positions of the methoxyl groups, it can be seen that the glucose portion of sucrose has its regular pyranose structure, but the fructose portion has a furanose structure. In sucrose then, the fructose OH group involved in ring formation is on the C_5 atom, whereas in fructose itself, the OH is on the C_6 atom. Therefore, the complete structure of sucrose is as follows:


Vertical structure

Haworth structure[a]

Sucrose

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[a] When the oxygen atom is drawn at the top of the furanose ring, OH groups drawn downward correspond to those on the left side of the vertical structure.

Since the carbon-attached group on the C_1 atom of glucose is fructose, sucrose may be called fructosyl glucoside. On the other hand, the group attached to the oside carbon of fructose (i.e., the oxygen atom of the bridge may be regarded as the oside oxygen of either sugar unit) is glucose; therefore, sucrose may also be called glucosyl fructoside. Furthermore, to indicate the ring size in the two sugar units, sucrose is more appropriately named α-D-glucopyranosyl-β-D-fructofuranoside or β-D-fructofuranosyl-α-D-glucopyranoside.

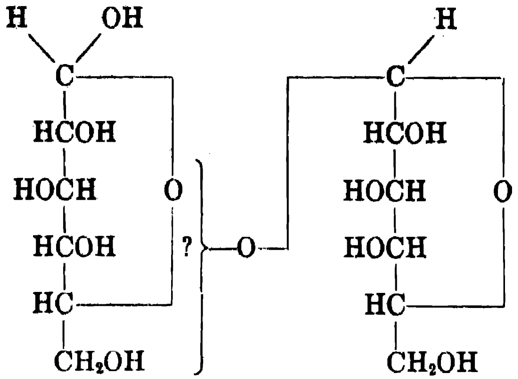
Sucrose is dextrorotatory, whereas a solution of its hydrolysis products is levorotatory. Because of this change in direction of rotatory effect, the hydrolysis mixture from sucrose is called *invert sugar*. D-Glucose is dextrorotatory ($[\alpha] = +52°$) to a smaller degree than D(−)-fructose is levorotatory ($[\alpha] = -92°$); hence an equal molar mixture of the two is levorotatory.

Sucrose is consumed in the United States in a greater amount than any other pure organic compound. Invert sugar is used in candy because it is sweeter than sucrose and chiefly because the mixture has less tendency to crystallize. In addition to its use as a food sweetening agent, sucrose is used to flavor medicines and as an antioxidant in many commodities.

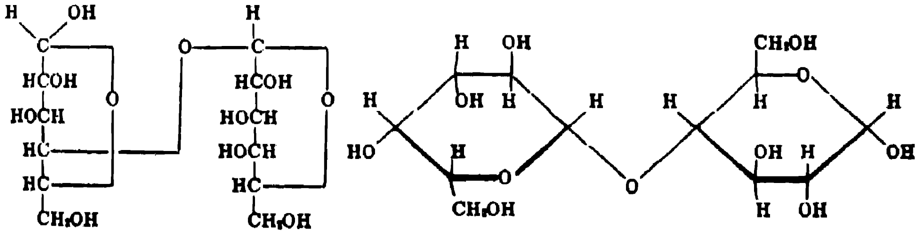
b. Lactose. Lactose, which is found in milk, has the same empirical formula as sucrose. It is used in baby foods and in pharmaceutical preparations. Its structure can be determined on the basis of the following facts: (1) Hydrolysis of lactose gives glucose and galactose.

$$\underset{\text{Lactose}}{C_{12}H_{22}O_{11}} + H_2O \xrightarrow[\Delta]{H_3O^+} \underset{\text{Glucose}}{C_6H_{12}O_6} + \underset{\text{Galactose}}{C_6H_{12}O_6}$$

(2) Lactose is a reducing sugar and forms a phenylosazone. Therefore, at least one potential carbonyl group is present, and also its α-OH group is free to form the osazone structure. One knows also that both carbonyl groups cannot be present because then the sugar units would have to be joined through an ordinary C—O—C bond. This is a typical ether structure which is not hydrolyzed in dilute acid. Since lactose is hydrolyzed in dilute acid, an acetal linkage rather than an ether linkage must be cleaved in the hydrolysis. Thus, the oside OH group of one sugar and a lower OH group in the chain of the other sugar unit are involved in bridging the two sugar units. (3) Hydrolysis of lactose phenylosazone yields glucose phenylosazone. Since phenylosazones are hydrolyzed with more difficulty than acetals, the osazone of lactose may be mildly hydrolyzed to cleave only the acetal linkage between sugar units. Then, whichever sugar unit was involved in osazone formation in lactose still has an osazone structure in the monosaccharide. Inasmuch as this turns out to be glucose phenylosazone, this much is known about the structure of lactose:

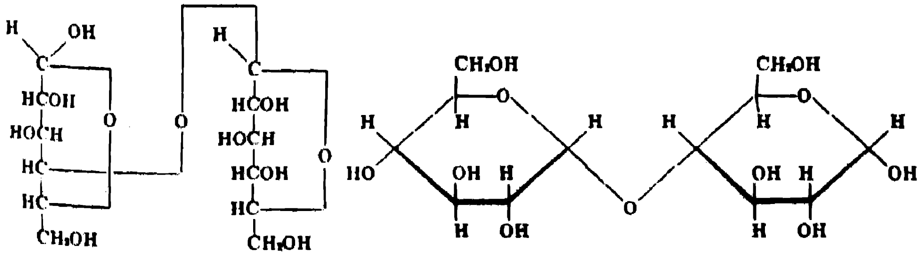


(4) Complete methylation of lactose and subsequent mild hydrolysis yields 2,3,6-trimethylglucose and 2,3,4,6-tetramethylgalactose. This means that the ring structure of the galactose portion of lactose has the pyranose structure, and that the OH of the glucose portion involved in the bridge between sugar units is the γ-OH. At least it must either be the γ- or the δ-OH, and on the assumption that the δ-OH is involved in the ring structure, the γ-OH must be involved in the intersugar acetal linkage. Therefore, lactose has the following structure:



Lactose (α-D-glucopyranosyl-β-D-galactopyranoside)

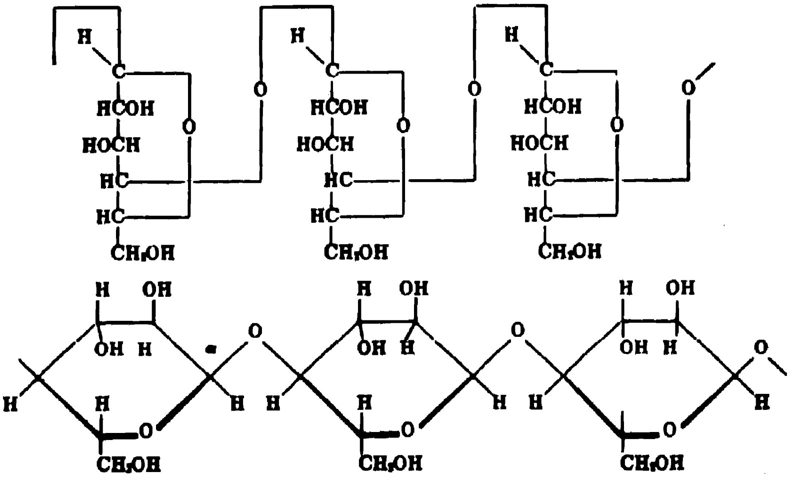
c. **Maltose.** Maltose is a disaccharide obtained in the partial hydrolysis of starch. It has an empirical formula $C_{12}H_{22}O_{11}$, is a reducing sugar, and produces two moles of glucose upon hydrolysis in dilute acid. It forms a phenylosazone and, upon complete methylation followed by hydrolysis in dilute acid, 2,3,6-trimethylglucose and 2,3,4,6-tetramethylglucose are recovered. Maltose is hydrolyzed by maltase but not by emulsin; hence, it contains an α-glucoside link. By the same reasoning as was used for lactose above, the structure of maltose must be as follows:



Maltose
(α-D-glucopyranosyl-α-D-glucopyranoside)

23.4 POLYSACCHARIDES

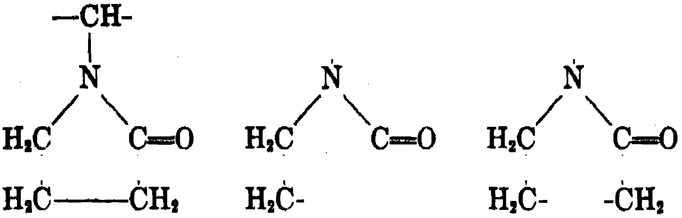
a. Starch. Starch is a polysaccharide found in all plants, especially corn, barley, potatoes, and cereal grains. It is present as small granules and, when heated with water, a colloidal solution is formed, in which a portion of the starch is in solution. The water-soluble fraction is called amylose, has a molecular weight in the range 50,000 to 200,000, and gives a blue color with iodine. The water-insoluble fraction, called *amylopectin*, amounts to 80 to 90 per cent of the starch granules, has a molecular weight in the range 70,000 to 1,000,000, and gives a red color with iodine. Both fractions have the empirical formula $(C_6H_{10}O_5)_n$. Upon acid hydrolysis, amylose and amylopectin yield glucose. Since starch does not exhibit carbonyl properties, the potential carbonyl groups must be tied up in joining the sugar units.



A segment of the starch molecule

When starch is hydrolyzed in the cell by enzymes, it is broken into smaller molecular fragments called *dextrins*, until it gets down to the dimer, maltose. Amylopectin differs from amylose not only in molecular weight, but also in the fact that all the glucose units are joined 1,4 in amylose (shown above), whereas amylopectin has some 1,6 linkages as well as 1,4 linkages. In other words, some of the intersugar bridges are between the C_1 atom of one sugar unit and the C_6 atom of the next sugar unit. In both fractions, the glucose units have the α configuration.

In a national emergency such as a war, it is impossible to collect and prepare enough blood plasma to treat those suffering from shock, burns, or other injuries. Fortunately, blood plasma substitutes have been found, the two most successful being polyvinylpyrrolidone (PVP) and dextran. PVP, a polymer of vinylpyrrolidone, was preferred by the British; dextran was preferred

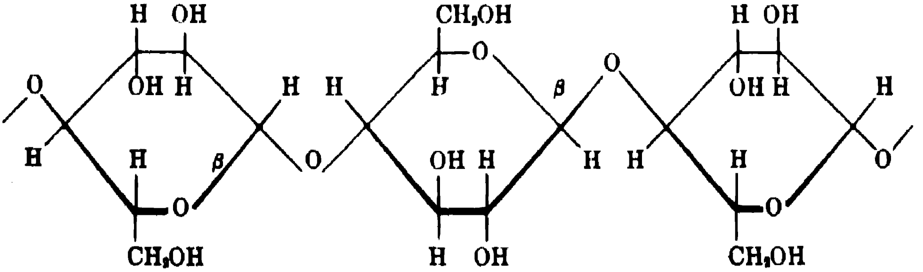


Segment of the polyvinylpyrrolidone molecule

by the military in the United States. Dextran is a polysaccharide, differing from starch by having α-1,6 linkages between glucose units. It is produced by fermenting sucrose to a polysaccharide of molecular weight near 40 million, then this is partially hydrolyzed to fragments in the molecular weight range 60,000 to 250,000.

Polysaccharides of extremely large molecular weight are insoluble and form the cell framework of plants. However, polysaccharides of lower molecular weights may be stored as a reserve supply of carbohydrates. One of the polysaccharides in plants, called *inulin*, has the same molecular formula as starch, but has a molecular weight of about 5000. It gives no more than a pale yellow color with iodine. Upon hydrolysis of inulin, fructose and a small amount of glucose are obtained. Carbohydrate is stored in animals in the form of *glycogen*. It has a molecular weight around 2000 and gives a red coloration with iodine. Upon acid hydrolysis, it yields glucose.

b. Cellulose. Cellulose, $(C_6H_{10}O_5)_n$, is the most abundant of polysaccharides, constituting 50 per cent of wood cells. Cotton and filter paper are almost pure cellulose. The molecular weight of cellulose is approximately 300,000. Complete hydrolysis of cellulose yields glucose, but partial hydrolysis gives *cellobiose*. Cellobiose is a disaccharide similar to maltose but with a β-glucoside configuration. This shows that cellulose consists of long chains of glucose molecules joined together by β-1,4 linkages.



A segment of the cellulose molecule

Cellulose serves as a raw material for a large quantity of commercial products. The cellulose may be extracted from wood by alkali extraction with sulfite or sulfide, as is done in the production of paper, or the cellulose may be used in the form of cotton. Having three OH groups per sugar unit, cellulose is a polyhydric substance in which at least one of the OH groups is more acidic than in a normal alcohol. Cellulose may be esterified with nitric acid in the usual manner of making nitrate esters to yield a "dinitrate" and a "trinitrate." The dinitrate has an average of two OH groups esterified per sugar unit, and the trinitrate has essentially all OH groups nitrated.

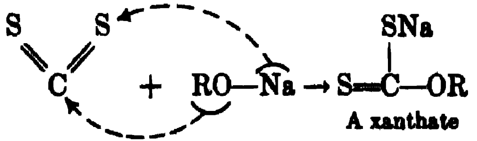
Cellulose dinitrate, called *pyroxylin*, is insoluble in ether and in alcohol, but when these two solvents are mixed in equal volumes, the solution will dissolve cellulose dinitrate. The resulting solution, called *collodion*, is sold at the drugstore. Nicknamed "new skin," it can be used for forming a protective film over skin abrasions and cuts. When spread on the wound, the solvent quickly evaporates to leave a colorless, transparent film. It is very flammable, so its use as a cement has been replaced by solutions of other polymers. Solutions of pyroxylin in esters and ketones are used as lacquers. Upon heating collodion with camphor, a gelatin is produced that thickens to a plastic material called *celluloid*. This was the first commercial plastic material. It darkened with age, burned with a very offensive odor, and was far inferior to present products. Cellulose trinitrate, *gun cotton*, is used as a propellant.

Cellulose may be acetylated to a diacetate and a triacetate by treatment with acetic anhydride in the presence of sulfuric acid catalyst. Called *Celanese* by some companies, cellulose acetate is dissolved in acetone, and the solution is used as a cement or a seal in constructing model airplanes.

Cellulose acetate is dissolved in methylene chloride-alcohol solvents and then poured on large, heated rollers. The solvent quickly evaporates, leaving a film, which is continually rolled off, pressed between more rollers to remove the last traces of solvent and air bubbles, and cut into sheets of varying sizes. This is used for photographic film and safety glass.[4] It is much less flammable and has a greater tensile strength than collodion films.

When cellulose acetate solutions are forced out of a tube called a spinneret, which is a tube closed at the end except for tiny orifices, the solvent rapidly evaporates to leave fine filaments. These are continuously pulled and stretched to prevent curling up, and the fibers are called *acetate rayon*. Acetate rayon has certain advantages over cotton for textiles, such as greater tensile strength and gloss. Many cigarette filters are made out of cellulose acetate in the form of a ropelike material with thousands of tiny parallel filaments.

Sodium hydroxide solutions of cellulose react with CS_2 to form xanthates.



R = cellulose residue

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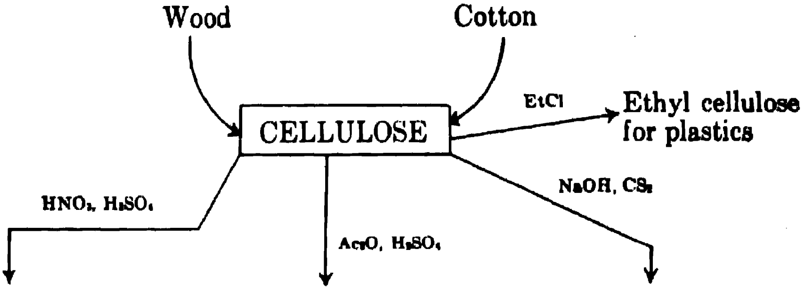
[4] One type of safety glass is manufactured by pressing two plates of glass together with a sheet of cellulose acetate between them. This prevents the glass from flying about when shattered.

The alkali solution of xanthate is a viscous, colloidal solution called *viscose*. When viscose is treated with acid, it decomposes to regenerate the cellulose. If this viscose is forced through a spinneret into an acid solution, cellulose fibers are formed. This is called *rayon* and is used for producing a textile offering some advantages over ordinary cotton. Note that its chemical composition, however, is still that of cellulose. It merely has different physical properties. When the viscose is extruded on to rollers in an acid medium, films are deposited, called *cellophane*. Cellophane is used as packaging material.

Cellulose may also be reacted with ethyl chloride to form ether groups out of the OH groups. The product, ethyl cellulose, is used for making plastics, which are discussed in Chapter 26.

The following chart summarizes the several uses of cellulose.



PYROXYLIN	CELLULOSE DIACETATE	XANTHATE
1. Solution in Et_2O + EtOH called collodion	1. Solution in acetone used as a cement	1. Spinneret in acid for rayon
2. Solution in esters and ketones used as lacquers	2. Spinneret for acetate rayon and cigarette filters	2. Pour on rollers in acid for cellophane
3. Formerly gelatinized with camphor to produce Celluloid	3. Roll out on warm rollers for safety film and safety glass	

. . . .

CELLULOSE TRINITRATE
Used for gun cotton.

STUDY EXERCISES

1. Show the series of reactions one would use (a) to form glucose phenylosazone, (b) to convert glucose into fructose, (c) to convert fructose into glucose, (d) to change glucose into mannose, (e) to convert an aldohexose into an aldopentose, (f) to transform an aldohexose into an aldoheptose, (g) to prepare methyl fructoside from fructose, (h) to prepare 2,3,4,6-tetramethylgalactose.
2. How can one verify the pyranose structure of aldoses?
3. Explain how one could distinguish by qualitative test-tube experiments (a) sucrose from lactose and (b) cellulose from amylopectin?

4. Explain clearly what is meant by the terms (a) mutarotation, (b) Molisch test, (c) epimerization, (d) anomers.

5. What are the contributions of the C_1 carbons to the observed specific rotations of methyl fructosides? (See data on page 549.)

6. Name five commercial products manufactured from cellulose.

7. Of what significance is the fact that a certain hexose gives a dextrorotatory carboxylic acid lactone?

8. What chemical reactions prove the presence of OH groups in cellulose?

9. When two aldoses form the same phenylosazone, what is known about the relationship of their structures? Can one aldose be converted into the other?

10. Can a nonreducing disaccharide display mutarotation? Why, or why not?

11. How could one prepare ethyl alcohol from glucose?

12. Give the structural formula of cellobiose.

TEST QUESTIONS, Set 21

1. How many active and mesomeric isomers are there with the formula (a) $HOOC—(CHOH)_3—CH_2OH$; (b) $HOCH_2—(CHOH)_4—CH_2OH$; (c) $HO_2C—(CHOH)_7—COOH$?

2. How many OH groups are there in a compound whose molecular weight is 122, if 1.22 g of it are acetylated and 40 ml of 1.0 *N* NaOH are required to neutralize the liberated acid?

3. A 1.32-g sample of a mixture containing 60% galactose and 40% sucrose would precipitate what weight of phenylosazone?

4. Write the structure of (a) ethyl-α-D-glucopyranoside, (b) methyl tetramethyl-α-D-glucopyranoside, (c) ethyl tetramethyl-β-D-glucofuranoside, (d) 6-trityl-β-D-mannopyranose.

5. What minimum weight of phenylhydrazine would be required to convert the hydrolysis products from 17.1 g of sucrose into osazone?

6. A nonreducing disaccharide, $C_{12}H_{22}O_{11}$, gives mannose and galactose upon hydrolysis. What are three possible structures for the disaccharide if it is assumed that both sugar units have a pyranose form?

7. A certain methyl hexoside can be obtained in two forms whose specific rotations are +16° and +89°. The hemiacetal form of the hexose can be obtained in an α and β anomer too, the α form having a specific rotation of 72°. What will be the specific rotation of the β form?

8. From the specific rotations of α- and β-D-glucose, calculate the contribution of the body of the sugars to the observed rotations. How does this compare with the value obtained from the data on the methyl glucosides?

9. The specific rotation of α-maltose is +168°, and it is +118° for β-maltose. What is the contribution of the hemiacetal carbon atom to the observed specific rotation?

10. Explain the fact that aldoses reduce Tollens' and Fehling's reagents but do not restore the color of Schiff's reagent.

11. If one tried to make an ethyl acetal of glucose, why is it that only one ethyl group could be introduced?

12. When α-D-mannose, $[\alpha]_D^{20} = +29.3°$, is dissolved in water, the optical rotation decreases as β-D-mannose is formed until at equilibrium $[\alpha]_D^{20} = 14.2°$. When β-D-mannose, $[\alpha]_D^{20} = -17.0°$, is dissolved in water, mutarotation occurs until $[\alpha]_D^{20} = 14.2°$. From these data, what is the percentage of the β form in the equilibrium mixture?

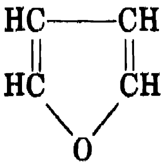
24

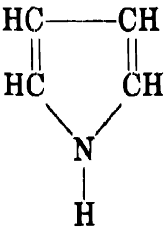
Heterocyclic Compounds and Alkaloids

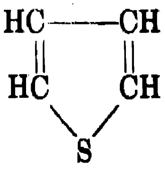
Again, time permits only a cursory discussion of an important topic in organic chemistry. According to the classification of organic compounds given in Section 1.3, heterocyclic compounds are those in which there is at least one ring containing one or more atoms other than carbon. We have already encountered some heterocyclic compounds, such as the lactones, lactams, hemiacetal, and acetal forms of sugars, phthalimide, and saccharin. However, the rings in these compounds are easily opened and closed by reversible reactions. They therefore have many of the same general properties as the respective open-chain compounds. On the other hand, there are some heterocyclic rings which resist opening, and remain intact through vigorous reactions, as do the benzene and cyclohexane rings. Normally, then, reference is made to this type of ring when the term *heterocyclic compound* is used. The ring may or may not have aromatic character. Many types of heterocyclic rings contain more than one hetero atom, e.g., dioxane.

24.1 FIVE-MEMBERED HETEROCYCLIC RINGS

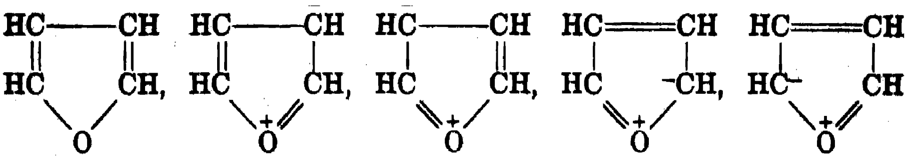
The most common of the five-atom heterocyclic rings are those of furan, thiophene, and pyrrole; each has some aromatic character as a result of resonance.







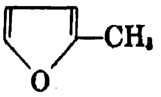
	Furan	Pyrrole	Thiophene
Resonance energy (kcal/mole)	17	21	30



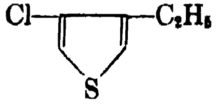
Resonance forms of furan

Analogous forms may be written for the thiophene and pyrrole rings. The aromatic character of these compounds is shown by the fact that they do not exhibit the typical olefinic properties of addition, polymerization, and easy oxidation. Thus, these compounds undergo substitution rather than addition reactions, and carbon-attached side chains may be oxidized by permanganate to a COOH group without oxidizing the ring.

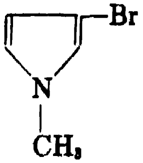
The positions in the rings are numbered clockwise or counterclockwise, starting with the hetero atom. Also, the positions may be referred to by Greek letters.



α-Methylfuran
or
2-methylfuran

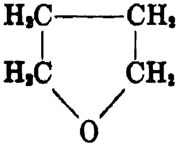


3-Ethyl-4-
chlorothiophene

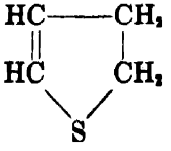


N-Methyl-3-
bromopyrrole

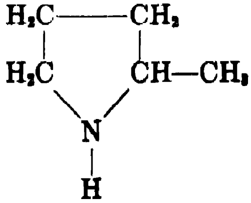
When the furan and thiophene rings are saturated, hydrogen atoms are regarded as substituents. A saturated pyrrole ring is called pyrrolidine.



Tetrahydrofuran

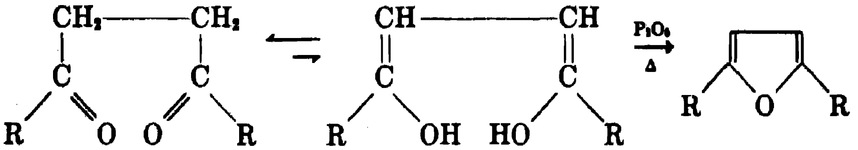


α,β-Dihydrothiophene

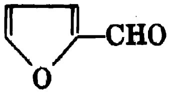


2-Methylpyrrolidine

a. Furan. The furan ring can be made by the dehydration of a 1,4-diketone:

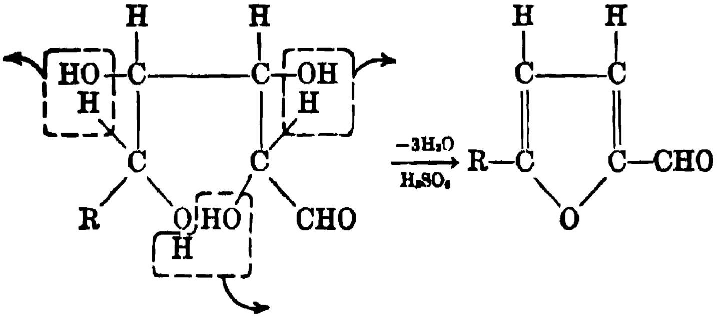


A common derivative of furan is furfural:



Furfural, or furfuraldehyde

Furfural is produced by treating cereal grains with sulfuric acid, followed by steam distillation to remove the furfural. Pentoses in the grain are dehydrated and cyclicized by the action of sulfuric acid. This can be seen if the aldopentose structure is twisted around as shown below.



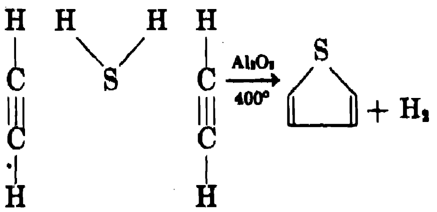
Similarly, polyhexoses in the grain yield hydroxymethylfurfural. This is believed to be the basis of the Molisch test, wherein the furfural or substituted furfural gives a deeply colored dye with naphthols and sulfuric acid.

In alkaline media, furfural is a typical aromatic aldehyde. Thus, it undergoes the benzoin condensation and the Cannizzaro reaction. In acid media, the ring is easily opened, the reaction being a typical acid-catalyzed hydrolysis of a vinyl ether to a carbonyl group. Furfural is used as a solvent, as a fungicide, and for making resins of the phenol-formaldehyde type.

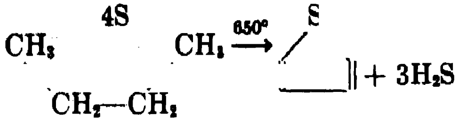
b. Thiophene. Thiophene itself is a colorless liquid with a boiling point (84°) and an odor very similar to that of benzene (b.p. 81°). Both compounds are present in coal tar and shale oil and, because of the nearness to each other of their boiling points, benzene obtained from these sources usually contains thiophene as an impurity. When benzene is used as a solvent for reactions, such as the Rosenmund reduction, any thiophene present would poison the catalyst; hence, thiophene-free benzene must be used. Impurities of thiophene in benzene are removed by shaking the benzene with sulfuric acid. The thiophene reacts much faster than benzene with sulfuric acid to form the soluble thiophenesulfonic acid.

Thiophene is produced by several reactions, two of which are as follows:

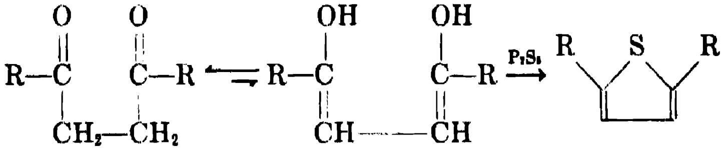
(a) From acetylene and hydrogen sulfide.



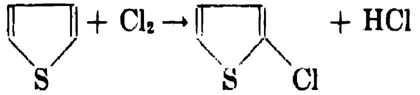
(b) From *n*-butane plus sulfur

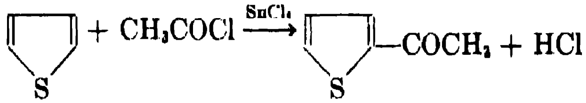


A general method of preparing thiophene derivatives, aside from nuclear substitution, is by heating 1,4-dicarbonyl compounds:

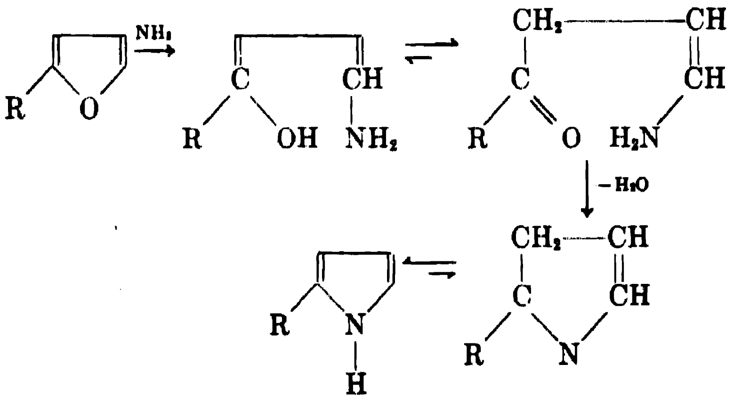


The thiophene ring undergoes electrophilic substitution reactions more readily than does the benzene ring. Thus, halogenation needs no catalyst, and milder acids than $AlCl_3$ may be used for Friedel-Crafts reactions:



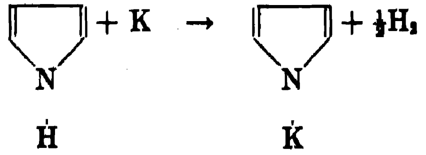


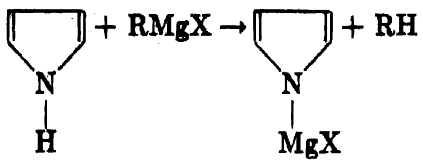
c. **Pyrrole.** Pyrrole itself is obtained from coal tar. Some of its derivatives can be made from the corresponding furans with ammonia:



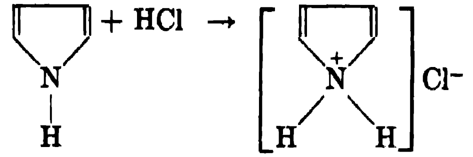
Although pyrrole is a secondary amine, it has weak acidic and weak basic properties:

Acid character:

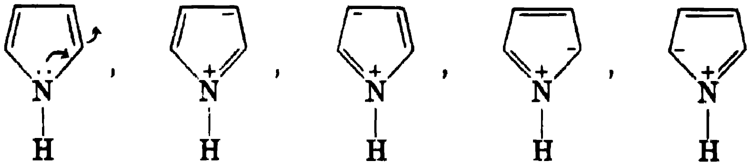




Basic properties:

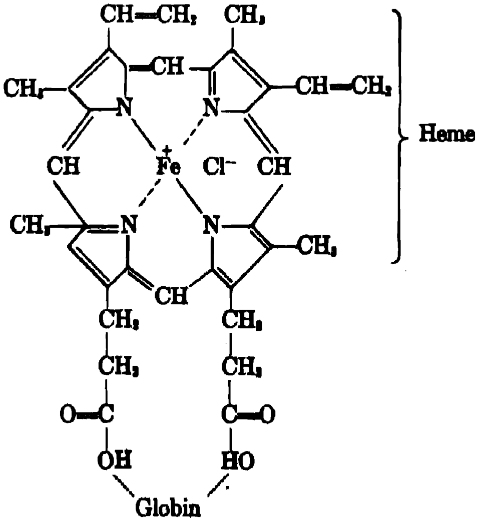


This amphoteric character is understandable in terms of resonance theory. The charge distribution in the ionic forms of pyrrole allows the hydrogen atom to be removed more easily than that of an aliphatic secondary amine and at the same time makes the unshared pair of electrons on nitrogen less available than in aliphatic amines.

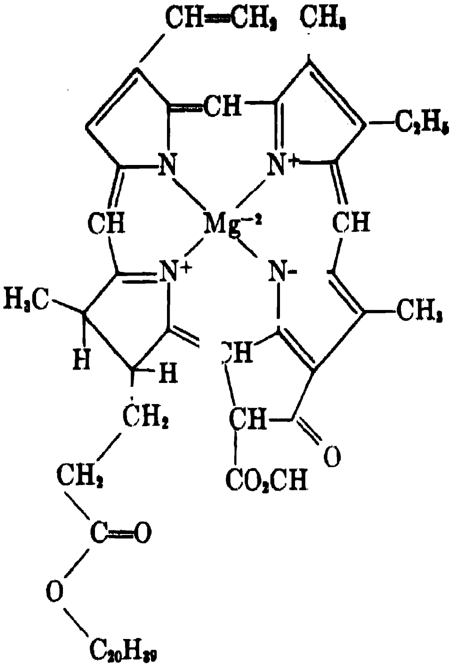


Thus, pyrrole has a K_b of about 10^{-14}. In contrast to this, the saturated compound, pyrrolidine, for which such resonance is not written, has a $K_b \sim 10^{-3}$.

Two important biological constituents are formed from the pyrrole ring. In hemoglobin and chlorophyll, there are four pyrrole rings connected by a conjugated system of carbon atoms and a metal ion. Hemoglobin has a ferrous ion, and chlorophyll has a magnesium ion.



Hemoglobin



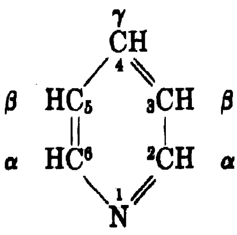
Chlorophyll *a*

Green plant pigment and photosynthesis catalyst

These structures need not be memorized. They are given here merely for inspection. The ferrous ion in heme is capable of absorbing oxygen reversibly, by which manner it carries and releases oxygen to the cells from the lungs. The heme structure is fairly planar and holds oxygen atoms between planes of hemoglobin molecules.

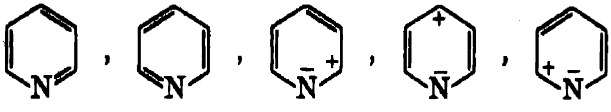
24.2 SIX-MEMBERED HETEROCYCLIC RINGS

a. **Pyridine.** The pyridine nucleus is obtained by replacing a CH of benzene by N:



Pyridine

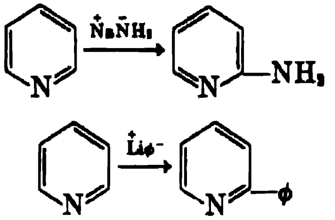
The positions of the ring are numbered or lettered as shown. The ring has the Kekulé resonance like benzene; however, the five carbons do not have identical electron densities as do all of the carbons of the benzene ring. Nitrogen is more electronegative than carbon, making certain ionic structures more stable than others.



Kekulé structures Ionic structures

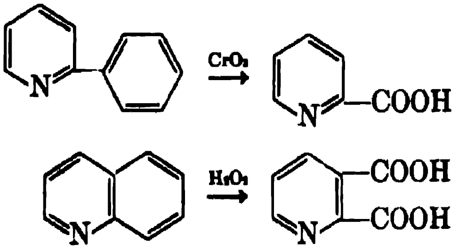
Resonance of the pyridine nucleus

Hence, nucleophilic reagents react more readily with the pyridine nucleus than do electrophilic reagents, especially at the 2- and 4- positions. For instance, pyridine reacts with nucleophilic agents at moderate temperatures:



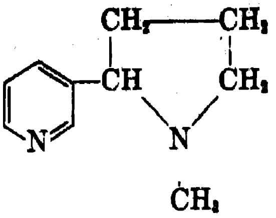
In contrast to this, pyridine is brominated, nitrated, or sulfonated only at very high temperatures, 300–400° and then at the 3 position.

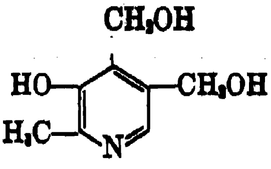
The pyridine ring resists oxidation by some agents even more than does a benzene ring. For illustration, in the oxidation of α-phenylpyridine and quinoline, the benzene ring suffers cleavage rather than the pyridine ring:



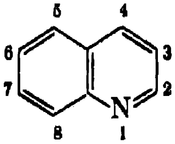
As a result of the charge distribution and stabilizing effect of the resonance of pyridine, it is a weaker base ($K_b \sim 10^{-9}$) than are aliphatic amines. The weak basic character of pyridine cannot be attributed to its ring structure, because the completely hydrogenated compound, piperidine, has a much larger K_b ($\sim 10^{-3}$). Nevertheless, pyridine is sufficiently basic to be alkaline to litmus and to form salts with dilute solutions of strong acids. It is completely miscible with water and is a fairly good ionizing solvent. It is also soluble in most polar organic liquids. Pyridine has a nauseating, persistent odor. It is obtained from coal tar in the middle oil fraction.

The pyridine nucleus is found in many physiologically active substances, such as nicotine and vitamin B_6.


Nicotine

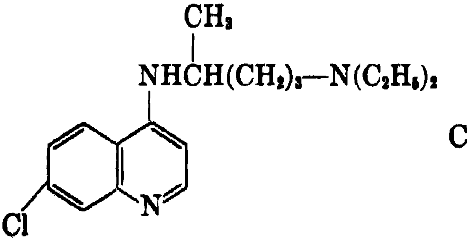

Pyridoxine
(vitamin B_6)

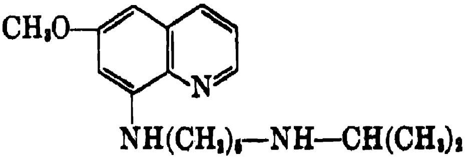
b. Quinoline. Quinoline has a structure similar to naphthalene, in which an N has replaced an *alpha* CH:


Quinoline

It has the Kekulé resonance of naphthalene and is typically aromatic. Its properties resemble those of pyridine in the same sense as the properties of naphthalene resemble those of benzene.

The quinoline nucleus is found in some physiologically active substances. For example, many of the 15,000 compounds synthesized and tested for antimalarial action during World War II were quinoline derivatives, and two of the most effective substitutes found for quinine are quinoline derivatives.

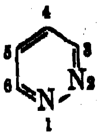

Chloroquine


Pentaquine

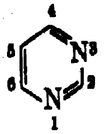
8-Hydroxyquinoline (oxine) is a highly useful agent in analytical chemistry, as mentioned in Section 19.3b.

24.3 MISCELLANEOUS HETEROCYCLICS

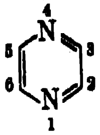
In addition to those discussed previously, other types of heterocyclic rings are possible, particularly those containing more than one hetero atom. Some illustrations are given below in the form of important representative compounds, and others are found in Section 24.4 and Chapter 25.



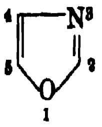
Pyridazine



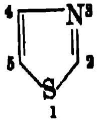
Pyrimidine



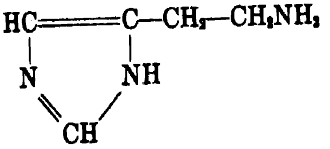
Pyrazine



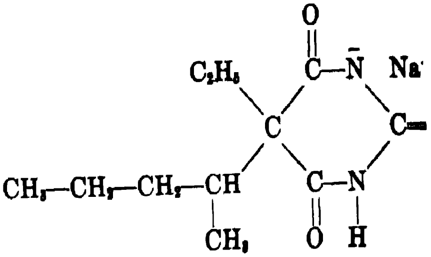
Oxazole



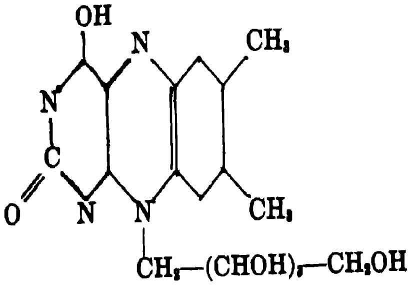
Thiazole



Histamine
Present in all cell tissue and associated with many allergies.



Sodium pentothal
A barbiturate, used as a general anesthetic by intravenous injection.



Riboflavin
Vitamin B_2

24.4 ALKALOIDS

The term *alkaloid* (alkali-like) is applied to a large group of basic, nitrogen-containing compounds found in plants. Most alkaloids are bitter, heterocyclic, optically active, and occur in plants as salts of organic acids (malic, citric, succinic, acetic, lactic, tartaric, oxalic, etc.). This classification is not all-inclusive because a few alkaloids such as berberine, papaverine, and pilocereine are optically inactive. A few alkaloids such as narcotine are found free in nature, probably because of their low basicity. Some alkaloids are found as glycosides of glucose and other sugars. A few alkaloids such as the yohimbine group, exist as esters of organic acids, whereas others are encountered as amides, such as the ergot alkaloids. Most alkaloids are bitter, and quinine is commonly used as the standard reference for bitterness in taste studies, but piperine from black pepper is tasteless. Alkaloids are commonly found among higher plants, although the ergot fungus produces alkaloids. Thus, it is difficult to give a definition to the term alkaloid which is without exceptions. A given alkaloid or group of alkaloids is usually found in only one or a few species of plants, and this characteristic excludes simple amines and amino acids from the alkaloid classification.

Many alkaloids are of great commercial importance owing to their powerful physiological action on animals. The occurrence and uses of some of the more common alkaloids are given in Table 24.1.

TABLE 24.1. OCCURRENCE AND USES OF SOME COMMON ALKALOIDS

Name	Source	Prominent Uses
Atropine	Belladonna	Dilate pupils of the eye
Caffeine	Coffee, tea	Stimulant
Cocaine	Coca leaf	Local anesthetic
Codeine	Opium	Analgesic (pain reliever)
Emetine	Ipecac roots	Induce vomiting
Lysergic acid diethylamide (LSD)	Ergot fungus	Produce delusions
Morphine	Opium	Analgesic; narcotic
Nicotine	Tobacco	Insecticide; stimulant
Pilocarpine	Jaborandi	Sweat producer
Quinine	Cinchona bark	Relief or cure of malaria
Reserpine	Rauwolfia (snake root)	Tranquilizer
Strychnine	Strychnos	Pesticide; alcoholism
Tubocurarine	Chondrodendron	Nerve paralysis
Yohimbine	Yohimbe bark	Sex stimulant

Alkaloids have served as medicines and poisons since early history. Opium has been used since the third century B.C. Atropine, once a familiar poison, is now used to dilate the pupils of the eye; physostigmine, used by West African tribes in certain rituals, is used as a bladder stimulant; curare, the South American arrow poison, is used by physicians as a muscle relaxant; seeds of the nux vomica, long used to destroy stray dogs and in gopher and rat poisons, is used to treat alcoholism and narcotic poisoning; since medieval days opium has been used by Orientals for the hallucination effect, and South American natives have chewed coca leaves for stimulation or cinchona bark for fevers. Alkaloids are active ingredients of many commodities used for pleasure or stimulation, such as coffee, tea, cocoa, tobacco, etc. Marihuana, incidentally, is not known to contain any alkaloids.

Chemical work on alkaloids dates back to 1803, when Derosne isolated a crystalline substance from opium. In 1805, a German apothecary, Serturner, independently isolated this same substance, purified and characterized it, and called it "morpheum." After his second paper in 1817 on morphine, chemists began to look for similar compounds. Thus, Pelletier and Caventou found strychnine in 1818 and brucine in 1819 in nux vomica, and in 1820 they isolated quinine and cinchonine from cinchona bark. There followed considerable speculation by early chemists about the chemical constitution of these compounds. By the middle of the 19th century, it was believed that several of the alkaloids contain in their structures the pyridine or quinoline molecules. It took the greater part of a century before the structures of some of the earliest discovered alkaloids could be worked out with confidence. That is, proposed structures from analyses are not regarded as conclusive until such a structure can be confirmed by its synthesis. Because of the complex stereochemical structures involved, syntheses of some of the alkaloids, which were completed only within the past 30 years, have become chemical classics.

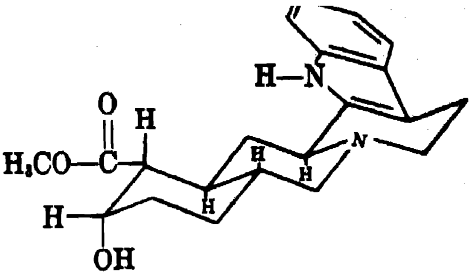
Opium is a dried exudation from a poppy grown in India, Egypt, Peru, and Turkey. The United States imports most of its supply from Turkey. Over 20 alkaloids have been isolated from opium, the most important of which are morphine, papaverine, codeine, narcotine, and thebaine. For years, morphine was the only good "pain killer" available, and hence it became indispensable in medicine and surgery. However, addiction to morphine and certain other alkaloids is such a serious social problem that the sale or possession of them is controlled by government agencies. As discussed in the chapter on chemotherapy, some of these natural products such as quinine and morphine have been supplemented or replaced by better, synthesized compounds. The relative pain-killing power of some analgesic drugs has been given the following rating (in arbitrary units):

Phenazocine	500–1000
Numorphan	500–1000
Dromoran	500–1000
Heroin	300
Morphine	100
Demerol	20–30
Codeine	15
Aspirin	1–2

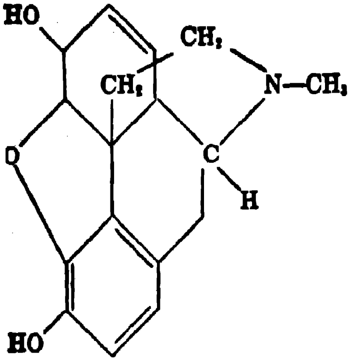
Aspirin is not an analgesic, but it is included for comparison because we are so familiar with it. The sale or possession of heroin is banned in the United States because of its addictive powers.

The function of alkaloids in plants is still unknown. Some experiments suggest that alkaloids are waste products from the nitrogen metabolism of plants, other work indicates that the alkaloids are not end products but metabolic intermediates. It has been proposed that alkaloids may serve to protect plants by discouraging animals from eating them because of their bitter taste or poisonous effect. Certain alkaloids may serve as metal-ion carriers through chelation. It is unlikely that any one theory will account for the functions of such a heterogeneous group of compounds.

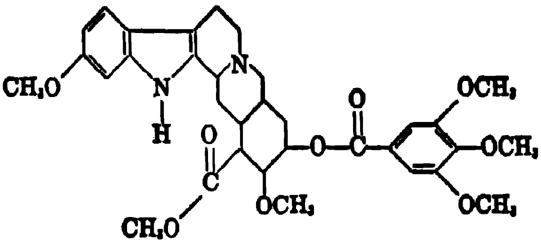
The study of the chemistry of the alkaloids has been fascinating to chemists because of the variety of their physiological effects on animals and the challenge they offer for structure determination and synthesis. The structures of some are given on page 570 for inspection; it can be seen that some of them are very complex.



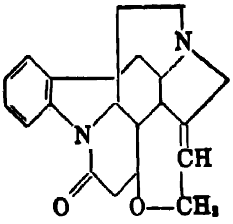
Yohimbine



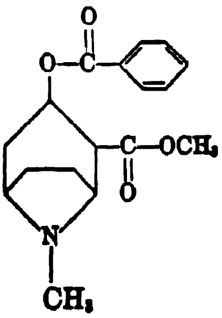
Morphine



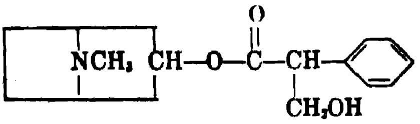
Reserpine



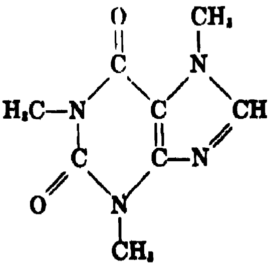
Strychnine



Cocaine



Atropine

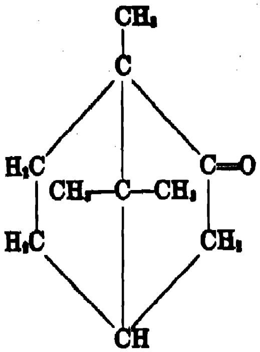


Caffeine

STUDY EXERCISES

1. Give the structural formulas for pyridine, quinoline, furan, thiophene, nicotine, pyrrole, and furfural.

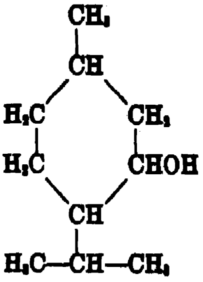
2. How could one distinguish by qualitative test-tube experiments (a) benzene



Camphor
(from wood of
camphor tree)

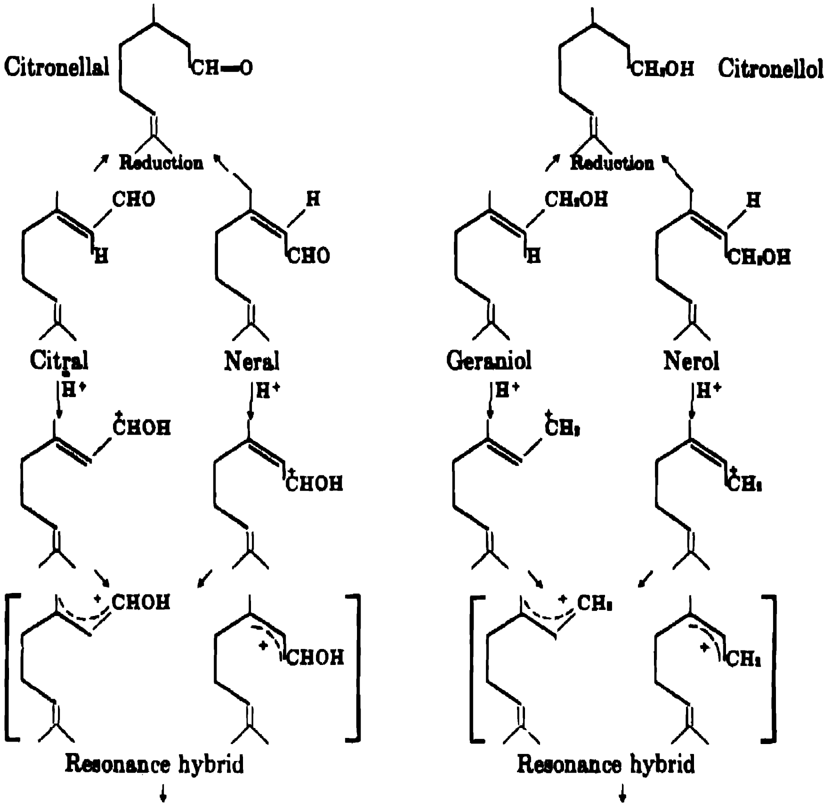
$$(CH_3)_2C{=}CH{-}CH_2CH_2{-}\underset{CH_3}{\underset{|}{C}}{=}CH{-}CHO$$

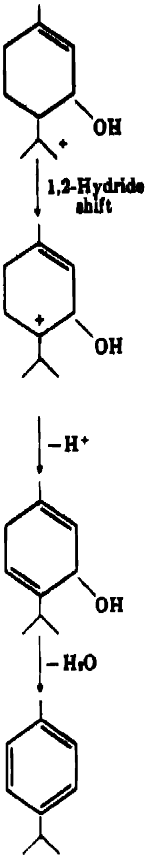
Citral
(from oil of lemon)



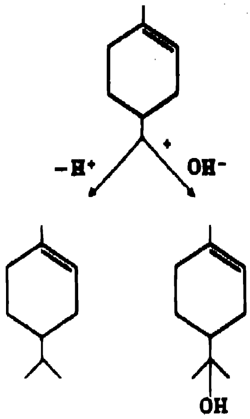
Menthol
(from peppermint oil)

Often the terpenoids are named after the plant from which they have been isolated, e.g., citronellol and citronellal from *oil of citronella*, and geraniol from *oil of geranium*. The terpenoids easily undergo oxidation or reduction and isomerization; terpenoids, consequently, are found to be simple variations of the same empirical formula:





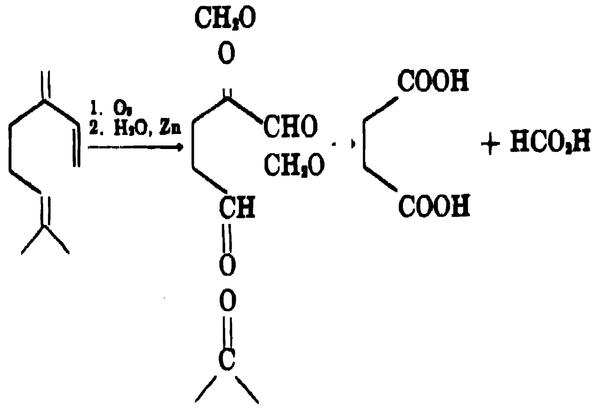
p-Cymene



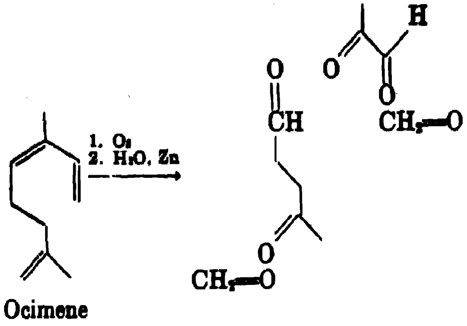
(±)-Limonene (±)-α-Terpineol

The determination of the structures and the synthesis of some terpenoids is sometimes rather simple, although the stereochemistry may be a problem.

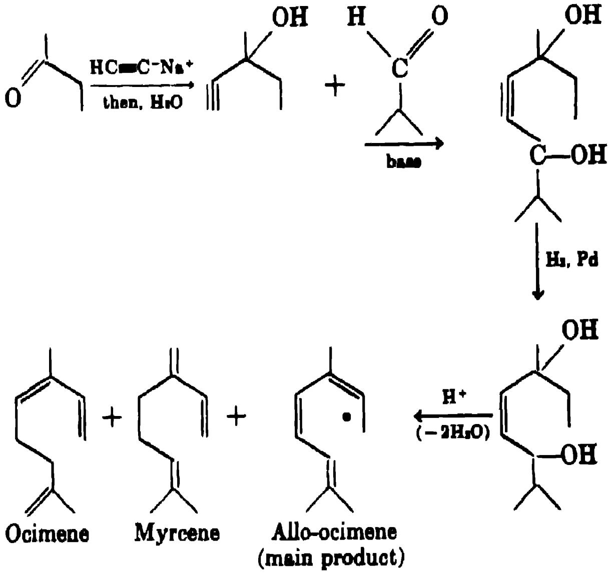
Degradation:



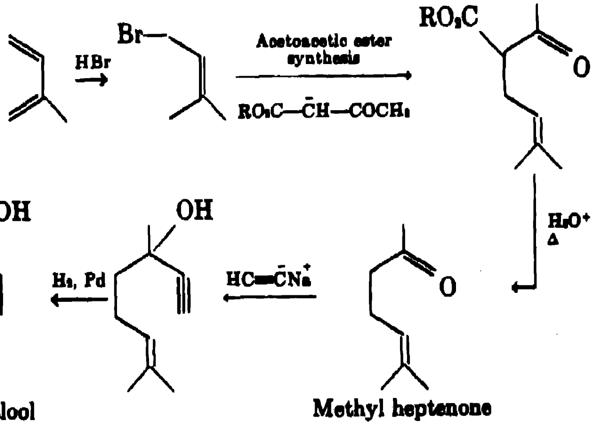
Myrcene



Synthesis:



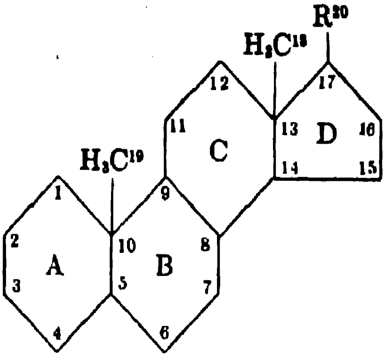
Another synthesis example:



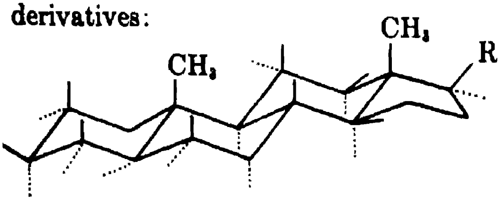
The higher terpenes have much more complex structures.

25.3 STEROIDS

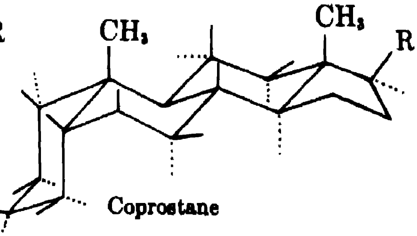
Steroids are found in nature, and their structures are based on the following ring system:



The structure consists of three cyclohexane and one cyclopentane ring fused together. The rings are puckered with *cis-trans* isomerism occurring at the ring junctions. The two principal series are the cholestane and coprostane derivatives:



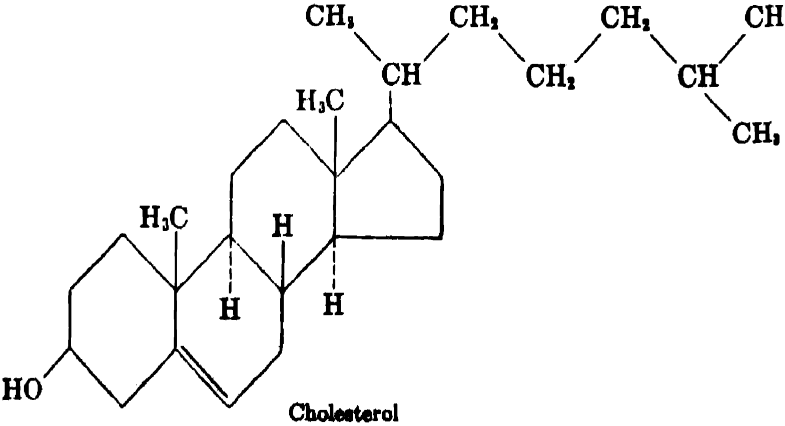
Cholestane



Coprostane

Notice that the rings are all *trans* at the ring junctions except for the A/B ring junction in coprostane, which is *cis*. The convention is to draw bonds below the general plane of the molecule (or behind the page) by a dotted line, designated α, and those on the opposite side by solid lines and designated β.

Hydroxy derivatives of steroids are called *sterols*, and the most common member is cholesterol:



Cholesterol

Cholesterol is present in all animal tissue cells but chiefly in the brain, nerve tissue, and renal glands. Cholesterol appears to play an important role in coronary heart disease.

The relation of diet to coronary heart disease and the correlation between cigarette smoking and lung cancer are two very controversial subjects in public health today. Several investigators report strong correlations between fat in the diet and atherosclerosis, while other authorities denounce the hypothesis for lack of proof.

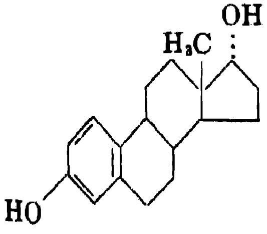
Nevertheless, there is increasing evidence that diet is one of the important factors in coronary heart disease. In this disease, fatty deposits form in the arteries which supply blood to the heart. These deposits consist of cholesterol, fat, and protein. The buildup of deposits takes years, but it may so constrict the artery that a blood clot may suddenly block the flow of blood (coronary thrombosis) and cause localized destruction of heart tissue.

What causes these deposits is the point of dispute. Most researchers agree that a high concentration of cholesterol in the blood is a contributing factor. All normal blood contains cholesterol, but little is derived directly from foods. The body synthesizes it in the liver from fats, carbohydrates, and proteins. Indications are that the type of fat in the diet is more important than the amount of fat. Patients fed only vegetable fats (corn, peanut, cottonseed oils), which are relatively unsaturated, have less cholesterol in their blood than those fed an equivalent amount of animal fat (beef fat, lard, butter), which are relatively saturated.

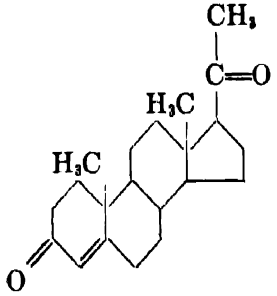
Although fats in the diet are getting the most attention in studies of atherosclerosis, other factors are also involved. For example:

1. *Heredity*—persons whose close relatives have had early cases are the most likely to get it.
2. *Sex*—cases among women between 35 and 54 are only one-sixth as frequent as among men in the same age range. Female sex hormones appear to reduce cholesterol deposits in the arteries.
3. *Obesity*—the blood cholesterol level increases with an increase in weight.
4. *Exercise*—exercise helps maintain normal levels of blood cholesterol and increases blood circulation to the heart to offset the effect of narrowed arteries.
5. *Stress and hypertension*—emotional stress, which causes the body to produce extra cholesterol, and high blood pressure may promote heart disease.

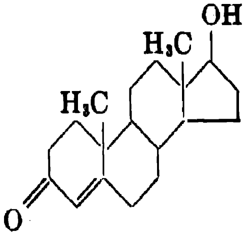
The sex hormones are steroid derivatives. The three most important are the female sex hormones estradiol and progesterone, and the male sex hormone testosterone.



Estradiol



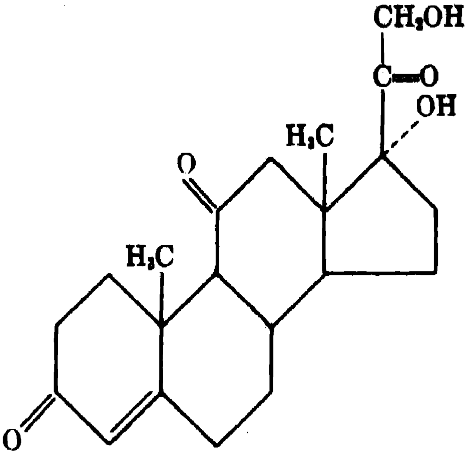
Progesterone



Testosterone

These hormones are responsible for the development of male and female sexual characteristics.

The steroids found in the adrenal cortex are important in controlling carbohydrate metabolism. Some of these, such as cortisone, are particularly active in relieving the symptoms of rheumatoid arthritis and asthma (cf. Section 28.2).

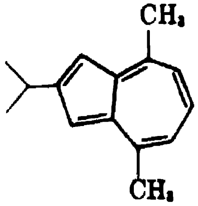


Cortisone

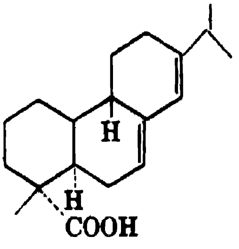
STUDY EXERCISES

1. Diagram the mode of addition of isoprene to form limonene, myrcene, and camphane.

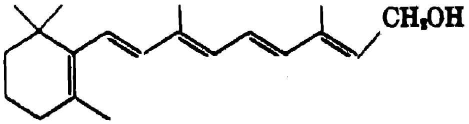
2. Show how the following structures may be put together from isopentyl carbon units:



Vetivazulene
$(C_{15}H_{18})$



Abietic acid



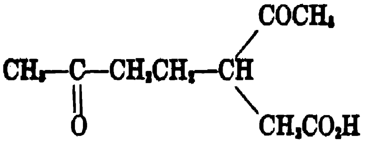
Vitamin A

3. What products would be recovered from the ozonolysis of citral and hydrolysis of the polyozonide?

4. Predict the relative stabilities of *cis* and *trans*-decalin in which each ring has a chair conformation, and give the basis of your prediction.

TEST QUESTIONS, Set 23

1. Hydrocarbon A, $C_{10}H_{16}$, found in citrus fruit peeling, adds two moles of hydrogen to yield *p*-menthane, $C_{10}H_{20}$. (a) How many rings are there in A? Oxidation of A by permanganate produces B. (b) Give two possible structures for A on this basis. Which is the more probable according to the isoprene rule? (c) What are the most likely structures for the monohydration product of A?

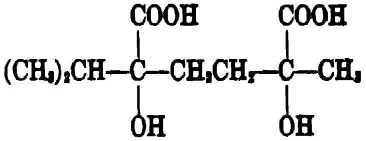


B

2. α-Terpinene, $C_{10}H_{16}$, adds two moles of hydrogen to form $C_{10}H_{20}$. Ozonolysis of α-terpinene yields C, whereas aqueous permanganate oxidation produces D.

$(CH_3)_2CH{-}CO{-}CH_2CH_2{-}CO{-}CH_3$

C



$$(CH_3)_2CH{-}\underset{OH}{\overset{COOH}{C}}{-}CH_2CH_2{-}\underset{OH}{\overset{COOH}{C}}{-}CH_3$$

D

(a) On the basis of these data and the isoprene rule, propose a structure for α-terpinene. (b) How do you account for the presence of OH groups in D?

26

Textiles and Plastics

26.1 NATURAL AND SYNTHETIC TEXTILES

Several important commodities, such as dyes, drugs, plastics, paints, rubber, and detergents, are synthesized rather than manufactured from natural raw materials. In terms of quantity, the textile industry is still based largely upon the natural fibers cotton and wool. However, the use of synthetic fibers is growing, and on a dollar basis, rayon, acetate rayon, and the completely synthetic fibers already hold more than 50 per cent of the textile market.

Cotton (cellulose) and wool (protein) are the major textile materials used in the United States. Linen, like cotton, is almost pure cellulose, but the fibers are longer and stronger than cotton. Silk filaments (protein) are sticky and hard to handle with machines; for this reason, not many silk fabrics are woven in the United States. Until 1884, these natural fibers were virtually the only ones used in textiles. In 1891, rayon made its commercial debut, and acetate rayon was introduced shortly before World War I. These two fibers are merely modifications of an already large molecular weight substance, cellulose. Not until 1938 was an entirely synthetic fiber used, and this was nylon.[1] Today the cellulosic man-made fibers account for 55 per cent of the synthetic textiles, and nylon alone is used for 40 per cent of all carpet fibers.

Textile Consumption	*1950*	*1961*
Man-made fibers	22%	31%
Cotton	68	61
Wool	10	8
	100%	100%

In the past decade, other synthetic fibers have become successful, particularly Dacron, Orlon, Lycra, Acrilan, and Herculon. The general advantages of textiles made from synthetic fibers are (1) high tensile strength and abrasion resistance; (2) resistance to mildew and insect attack; (3) low degree of water absorption, therefore, quick drying; and (4) dimension stability, i.e., they hold a manufactured crease but have little wrinkling or shrinkage. Two disadvantages of synthetic textiles which have presented problems to the industry are their tendency to accumulate static electricity and the poor dyeability of the nonpolar polymers such as polypropylene. These shortcomings have largely been overcome by the use of antistatic agents (sugar and polyhydric derivatives) and special dyeing techniques. For example, a pigment is frequently impregnated into the fiber, and this gives essentially the same appearance as a dyed fabric.

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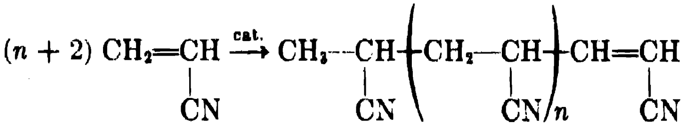
[1] Up to the early 1930's, little was known about what type of molecular structures make good textiles. Beginning in 1928, W. H. Carothers pursued pioneering studies in this area, and guided the lengthy research of Du Pont on polymers. Finally in 1938, nylon went into commercial production with phenomenal success.

26.2 POLYMERIZATION AND POLYCONDENSATION

The large molecules (macromolecules) synthesized for textiles, plastics, and rubber are made by polymerization or polycondensation reactions. Polymerization of alkenes was discussed in Section 3.4, where it was shown that free radicals, metal alkyls, or acids are used to catalyze the polymerization of alkenes. By this reaction, for example, acrylonitrile is polymerized to produce the giant molecules from which Orlon is made.



$$(n+2)\ CH_2{=}\underset{\overset{|}{CN}}{CH} \xrightarrow{cat.} CH_3{-}\underset{\overset{|}{CN}}{CH}\left(CH_2{-}\underset{\overset{|}{CN}}{CH}\right)_n CH{=}\underset{\overset{|}{CN}}{CH}$$

Polyacrylonitrile

Two common types of polycondensations for making macromolecules are polyesterification and polyamide formation. A dicarboxylic acid and a dihydric alcohol are allowed to form an ester, but because both ends of each molecule may react, the reaction takes place over and over to produce a macromolecule. Dacron is made by this reaction.[3] See page 584.

26.3 PLASTICS

Plastics have properties over a range between two extreme types. The *thermosetting* plastics will stand high temperatures, are resistant to chemicals, are hard to break or burn, and are not easily scratched. In contrast to these, the *thermoplastics* soften at moderately high temperatures, are more readily attacked by chemicals, burn easily, and are usually transparent. Because plastics may be produced having properties anywhere between these two extremes, they serve for the manufacture of many industrial and domestic commodities. Plastic articles are shaped by molding, extruding, or laminating processes. Warm, fluid plastic material may be forced into a hot or cold closed mold; or the mold may be filled with cold plastic material and then heat and pressure applied. For tubing and fibers, liquid plastic material is extruded from circular or pinpoint orifices into cold atmospheres. Laminates are manu-

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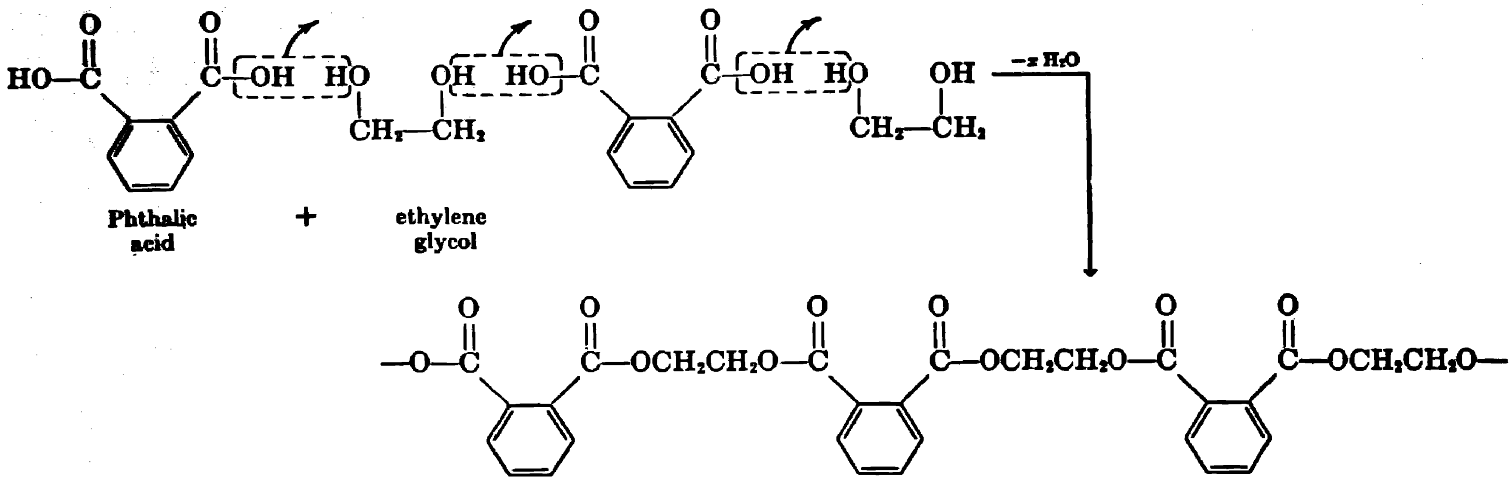
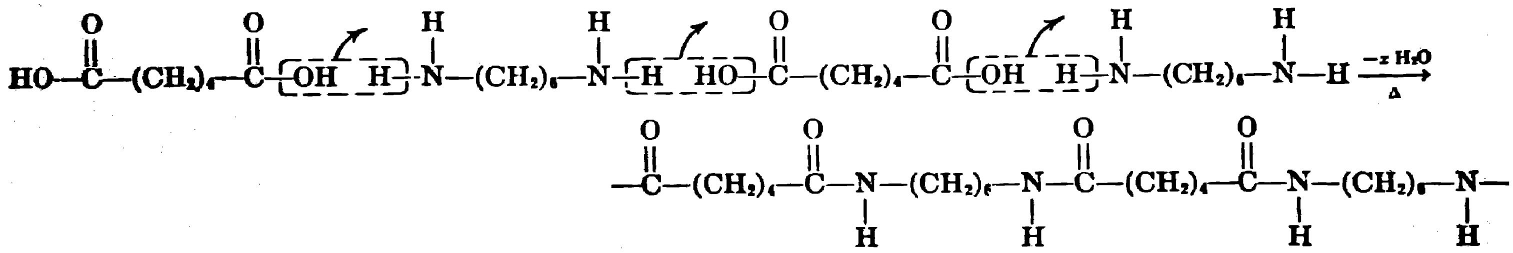
[3] In practice, the dimethyl ester of phthalic acid is used; it reacts with ethylene glycol to displace the more volatile methyl alcohol.



Segment of the Dacron molecule

When adipic acid is heated with hexamethylenediamine, polyamide formation occurs. This is the way nylon is produced.



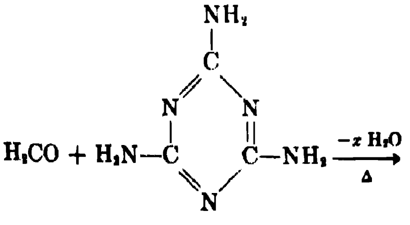
Segment of a nylon molecule

factured by soaking wood or cardboard in resins or plastic solutions and then applying pressure and heat. This gives the laminate the same texture throughout.

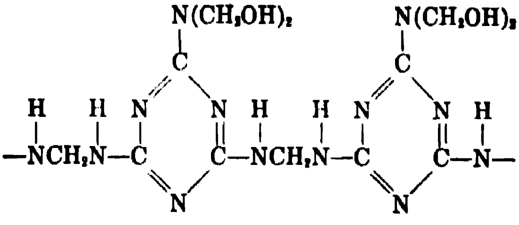
In the manufacture of plastic materials, usually certain low-melting substances are added to the polymers to impart toughness or flexibility. These additives, called *plasticizers*, are merely physical additions. Such substances as phthalic acid esters, phosphate esters, castor oil, or sulfonamides are used.

More and more of the markets once held by plywood, glass, and metals have been taken over by plastics, and the industry has doubled its growth every five years since 1930. About one-fourth of the plastics go into building products materials. The uses and more prominent features of plastics are summarized in Table 26.1. This table is by no means inclusive because the properties and uses of the various types of plastics overlap too much for each type to be uniquely characterized. Also, there are at least 20 major types of plastics with more than 130 trade names.

Note that most of the thermoplastics are produced by polymerization, whereas the thermosets are polycondensation products. The preparation of Bakelite was mentioned in Section 10.6. Melamine is a cyclic amine which polycondenses with formaldehyde.



Melamine



A segment of melmac polymer

The formation of the polyesters and polyamides was discussed in Section 26.3.

We saw in Section 9.6 that perfluoro compounds have unusual thermal stability and inertness to various reagents. Similarly, fluorocarbon polymers are especially stable. Polyethylene is usable as a polymer up to about 100°, whereas fluorocarbon polymers withstand temperatures above 300°. In fact, the properties of Teflon almost caused its abandonment. Ordinary molding equipment would not handle it because of its high melting point. There is no known solvent for it. Its slipperiness and immunity to "wetting" agents prevented its mixing with other materials or laminating. Finally there was found a way of handling it in the form of a dispersion of tiny needle-

TABLE 26.1. MAJOR CHARACTERISTICS OF PLASTIC TYPES

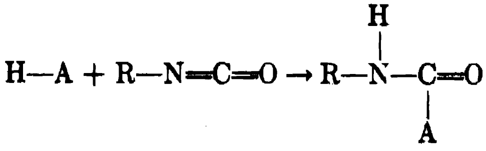
Type	Raw Materials for Production	Special Properties or Uses	Trade Names
		Thermosetting Plastics	
Formaldehyde	CH_2O	A polyacetal. Stiff, corrosion-resistant, good substitute for metals in car parts and plumbing fittings	Delrin, Celcon
	CH_2O + phenol	Tough and strong. Used for electric switch parts and cabinet panels	Bakelite
	CH_2O + melamine	Used to make dinnerware	Melmac
Polyester or alkyd	Phthalic or terephthalic acid plus ethylene glycol	Used to make car panels and bodies, knitted wear and typical wool uses as blankets, surface coatings, clothing	Dacron Mylar
Polyamide	Hexamethylenediamine plus adipic acid	High luster and tensile strength (4 times steel on a weight basis). Used for tire treading, knitted wear, marine ropes, parachutes, surgical sutures, carpeting, etc.	Nylon, Zytel Antron
Siloxane	CH_3Cl + Si	Heat and water repellent. Used for gaskets, heating baths, high temperature insulation coatings, safety-glass interlayers, and to waterproof surfaces and clothing	Silicones
Polyurethane	Glycols + diisocyanates	Elastic, abrasion resistant yarn. Used for "stretch" clothing and "spongy" articles	Lycra
		Thermoplastics	
Acrylics	Esters and sidechain derivatives of acrylic acid, $CH_2{=}CH{-}COOH$	Clear, transparent and shatter-resistant. Used for airplane windshields, dental bridges, medical instruments and blankets	Plexiglas, Lucite Acrylon

TABLE 26.1. Continued

Type	Raw Materials for Production	Special Properties or Uses	Trade Names
Cellulose family	Cotton plus acetic acid Cotton + HNO_3, H_2SO_4 Cotton + C_2H_5Cl	Used for toys, combs and brushes, movie film, draperies, cigarette filters	Celanese, Acele (acetate) Celluloid (nitrate) Ethocel (ethyl ether)
Vinyls	Vinyl chloride Vinyl cyanide Vinyl acetate	Flexible products. Used for outer garments, and for typical wool uses. Polyvinyl acetate used in do-it-yourself water-base paints.	Dynel (chloride + cyanide) Orlon (cyanide)
		Soil conditioners	Krilium (cyanide + hydrolysis)
	Vinylidene chloride $CH_2{=}CCl_2$	Auto seat covers, tubing and pipes, playing records.	Saran
Polystyrene	Styrene	Rigid products. Used for refrigerator insulation, cork substitute, translucent window panels	Styron
Polyethylenes	Ethylene	Flexible products. Used for lab ware, acid containers, plumbing	Polythene, Alathon
	$CH_3{-}CH{=}CH_2$	Carpeting, clothes	Herculon
	$CF_2{=}CF_2$, $CF_3{-}CF{=}CF_2$	Resistant to fuming HNO_3 and aqua regia, very insoluble, low wettability, low brittle and high melting points. Used for high-temperature paint-on lubricants, cables, gaskets, replacements for human arteries, and missile nosecones	Teflon
	$CF_2{=}CFCl$		Kel-F or Fluorothene

shaped particles. It is not surprising, then, to find *Teflon*-coated bearings and bushings that need no lubricant, and baking pans that need no greasing.

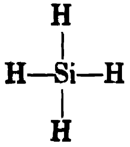
Another latecomer among the plastics is the polyurethane-type polymer. The isocyanate group N=C=O adds reagents having active hydrogen atoms according to the general equation



$$\mathrm{H{-}A + R{-}N{=}C{=}O \rightarrow R{-}\overset{H}{N}{-}\underset{A}{C}{=}O}$$

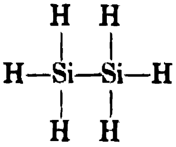
The polyurethanes offer many advantages of abrasion resistance, low water absorption, and good electrical properties. As foams, they have greater load-bearing capacity and resistance to oil and air deterioration than natural rubber. Because of this property, they make excellent pillows, table pads, cushions, mattresses, and structural support in aircraft frames.

Silicon is right under carbon in the periodic table and resembles carbon in having a covalency of four. It forms Si—Si as well as Si—C bonds. Thus, silicon may replace carbon in many simple molecules.



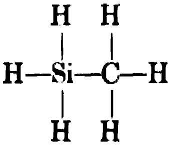
$$\mathrm{H{-}\overset{H}{\underset{H}{Si}}{-}H}$$

Silane



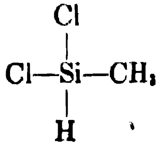
$$\mathrm{H{-}\overset{H}{\underset{H}{Si}}{-}\overset{H}{\underset{H}{Si}}{-}H}$$

Disilane



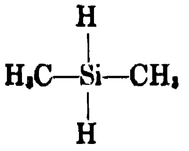
$$\mathrm{H{-}\overset{H}{\underset{H}{Si}}{-}\overset{H}{\underset{H}{C}}{-}H}$$

Methysilane



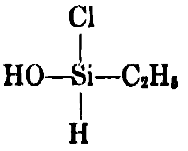
$$\mathrm{Cl{-}\overset{Cl}{\underset{H}{Si}}{-}CH_3}$$

Methyldichlorosilane



$$\mathrm{H_3C{-}\overset{H}{\underset{H}{Si}}{-}CH_3}$$

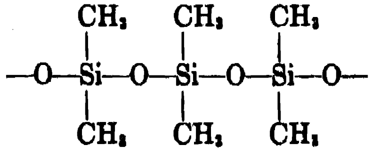
Dimethylsilane



$$\mathrm{HO{-}\overset{Cl}{\underset{H}{Si}}{-}C_2H_5}$$

Hydroxychloroethylsilane

In general, the silicon bonds are more polar than those of carbon. When dimethyldichlorosilane is reacted with cold water, it quickly hydrolyzes to give dimethyldihydroxysilane. This rapidly polycondenses, splitting out H_2O between two OH groups to give macromolecules, called *silicones*. First, high-boiling oils result, and as the polymerization proceeds, solids are formed.

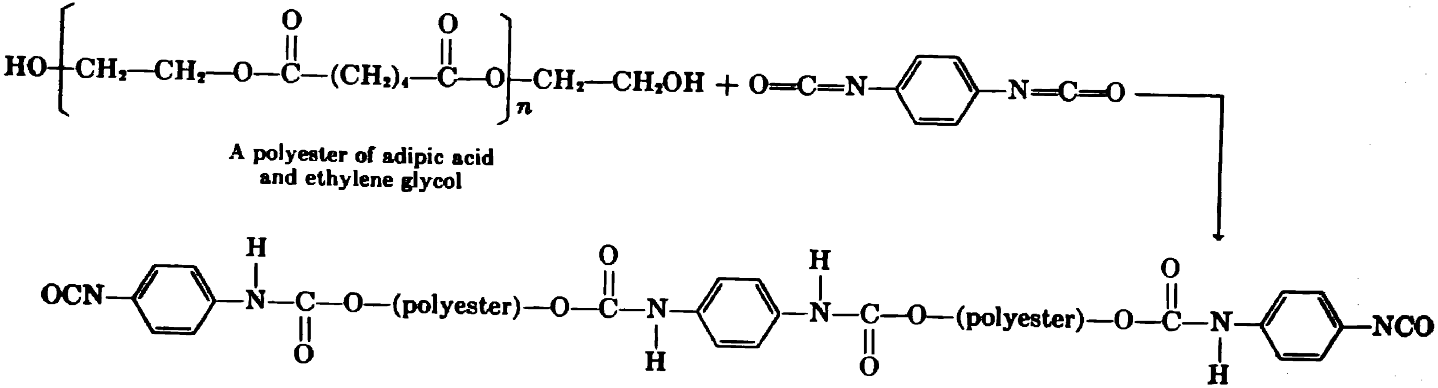


$$\mathrm{{-}O{-}\overset{CH_3}{\underset{CH_3}{Si}}{-}O{-}\overset{CH_3}{\underset{CH_3}{Si}}{-}O{-}\overset{CH_3}{\underset{CH_3}{Si}}{-}O{-}}$$

Segment of a silicone molecule

Polycondensation may be linear or in two dimensions, and if various groups are used in place of the CH_3 groups, products of a wide variety of properties

When low molecular weight alkyds (mol. wt. 2000) are reacted with diisocyanates, versatile polymeric materials are produced.



A polyester of adipic acid and ethylene glycol

Segment of a polyurethane molecule

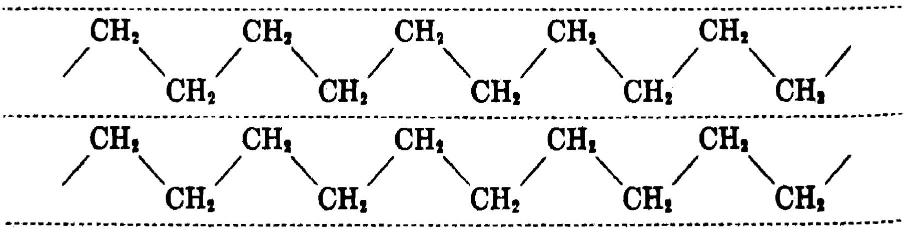
may be obtained. The use of perfluoro groups, for instance, gives products which will be unaffected by temperatures up to 800°. They are excellent for transparent safety-glass interlayers for supersonic jet aircraft.

Fluorocarbon resins are used in various missile types for insulation, gaskets, pump packing, fuel lines, etc. An Atlas missile and its launching gear, for instance, use about one ton of fluorocarbon.

When alcohols, alkyl halides, ethers, acetals, and some other classes of compounds representable by the symbol Y—Z are added to an olefin to be polymerized, the resulting polymer molecule will have Y at one end and Z at the other end, $Y{-}(CH_2CH_2)_n{-}Z$. The product is called a *telomer* (Gr. *telos*, end; *mer*, part). This process is used to control polymer size. Many telomers of ethylene are soft to hard waxes and are used in place of natural waxes, particularly for high-temperature applications.

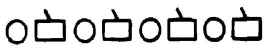
26.4 PHYSICAL PROPERTIES OF MACROMOLECULES

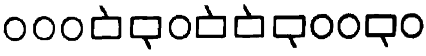
Macromolecules need to be high melting for some purposes and low melting for others. Rubbers are low melting, fibers for textiles are high melting, and plastics are in between. Polymer molecules may form an amorphous solid in which the molecules are entangled like "cooked noodles," or the molecules may form a crystalline solid in which the molecules are lined up approximately parallel like a strand of rope. Crystalline polymers are usually higher melting, and the crystallinity depends mainly upon the polar and steric relationships between the macromolecule chains. Intermolecular forces (van der Waals, dipole-dipole, or hydrogen bonds; cf. page 264) tend to bind the chains together, and the stronger these forces are, the more crystalline is the polymer. Thus, polymers of alkenes with low cohesive forces are amorphous and rubbery, whereas nylon and wool tend to be crystalline, owing to strong interchain hydrogen bonds between CO and NH groups. Plastics are between the amorphous and crystalline extremes, being amorphous but not elastic. If large groups extend out of the polymer chains, this, too, hinders the chains from lining up for a crystalline high melting polymer. For instance, polyethylene is crystalline, not because of large intermolecular forces, but because the molecules are very linear and allow close packing.

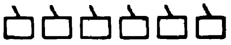


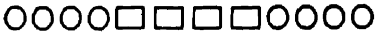
When the molecules can get close, the weak van der Waals forces become more effective. Polystyrene, on the other hand, has bulky phenyl groups reaching out to prevent close packing. Consequently, it is amorphous. The crystallinity of polymers can also be increased by certain physical treatments.

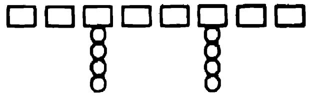
One of the reasons the use of synthetic fibers is increasing is that they can be manufactured to meet desired specifications. For instance, the new *isotactic* polymers produce strong, high-melting fibers for industrial applications. Isotactic polymers are those in which the monomer units are lined up in identical stereo orientations, and the chains are substantially free from branching. New techniques in polymerization have led to the production of polymers having specific arrangements of monomer units. Conventional methods yield the ordered or random arrangement of monomer units. In such copolymers, the blending of the monomers is very intimate and the polymer properties are an average of the properties of the two monomers. The isotactic polymers are produced with metal alkyl catalysts (cf. page 112), on whose surfaces the polymer molecules grow to form long, straight chains. In the block and graft copolymers, each monomer displays some of its unique characteristics; some of these properties will be an addition instead of an average property. For illustration, a graft copolymer of styrene and vinyl alcohol, consisting of a styrene backbone and branches of polyvinyl alcohol, is soluble in both water and toluene. The polyvinyl alcohol branches are readily solvated in water (page 261), with the result that the insoluble polystyrene portion is maintained in a state of stable suspension. In toluene, the polystyrene trunk is dissolved while the polyvinyl alcohol branches collapse and are kept in a state of stable suspension because of their attachment to the dissolved polystyrene trunk. The cross-linked polymers are produced by controlled radiation. It yields fibers which are more heat resistant, and less soluble and elastic.

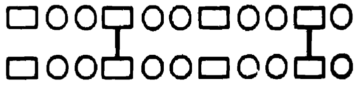

Ordered arrangement


Random arrangement


Isotactic polymer


Block copolymer


Graft copolymer


Cross linked polymer

Since the size and shape of macromolecules are major factors affecting their properties, it is important to have reliable methods of determining these characteristics. Although chemical methods give some information about the size of macromolecules, physical methods give more information about their spatial configurations. These methods involve measurements of (1) viscosity,

(2) osmotic pressure, (3) ultracentrifuge (sedimentation rate and equilibrium), (4) light scattering, (5) film balance, and (6) X-ray analyses. These methods may give different values for the same material, because such large quantities are involved that close agreement is difficult. Some methods are more effective for certain molecular sizes or shapes. For instance, light-scattering data will be more accurate the larger are the molecular weights. Values differing by less than 15 per cent are within experimental error, while differences greater than this are probably real.

STUDY EXERCISES

1. What are the raw materials or monomers used to produce (a) nylon, (b) Bakelite, (c) Dacron, (d) silicones, (e) Plexiglas, (f) Celanese, (g) Ethocel, (h) Dynel, (i) Orlon, (j) Krilium, (k) Saran, (l) Styron, (m) Polythene, (n) Herculon, (o) Teflon, and (p) Kel-F?

2. Which types of plastics would probably be used for (a) car panels and bodies, (b) oil gaskets, (c) knitted wear, (d) blankets, (e) soil conditioners, (f) auto seat covers, (g) dental bridges, (h) surgical sutures, (i) high-temperature paint-on lubricants, (j) flexible laboratory ware, (k) cork substitutes?

TEST QUESTIONS, Set 24

1. What resemblance is there in the structures of nylon and proteins?

2. What series of reactions could be used to produce adipic acid and hexamethylenediamine from butadiene?

3. What volume of 0.5 *N* KOH would be required to neutralize a 10-g sample of Krilium (polyacrylic acid) of molecular weight 36,000?

4. What volume of 2.0 *N* HCl would be required to neutralize the ammonia released from the hydrolysis of a 2.65-g sample of polyvinylcyanide of molecular weight 53,000?

5. How could one distinguish by qualitative test-tube experiments (a) a piece of nylon from a piece of cotton fabric; (b) a piece of rayon from rayon acetate fabric?

6. One type of plastic is prepared by polymerizing esters of methacrylic acid, $CH_2{=}C(CH_3){-}COOR$. Indicate the series of reactions one could use to prepare methacrylic esters if methyl and ethyl alcohols were the only sources of organic substances.

27

Dyes and Dyeing

Man has always enjoyed color, yet it is only within the last century that it has been possible for him to wear clothes dyed any color of the rainbow. One is inclined to think of ancient or medieval times as having many bright, deep colors; but actually the variations in color were relatively few, and the high costs of dyes restricted their use to royal or rich families. Color is something everyone enjoys and takes for granted, but even the lowest-income groups enjoy variations today that were unavailable to kings a century ago. How dreary the world of colonial days would appear to us now!

Color is utilized in several ways other than for its esthetic value. The right combinations of colors in business are very important. In one case, for example, meat looked very dark in a certain butcher shop with yellow walls and yellow sawdust. When the walls were repainted a light blue, and green sawdust was used, the meat had a red, fresh-meat color, and sales increased severalfold. Color is increasingly being called upon to help sell products. Color schemes are used in industry to mark dangerous zones, to label various receptacles, to indicate the direction of flow of traffic in buildings, etc. Proper color schemes not only provide better visual conditions, but also raise morale, speed up production, and affect safety records. Before the dyes are discussed, it would be profitable to consider the basic principles of color.

27.1 COLOR AND THE VISIBLE SPECTRUM

The basic characteristics of light were discussed in Sections 6.3 and 17.1. When a beam of white light passes through a glass prism, it is dispersed into bands of colors. The rays of longest wavelength, found at one end of the visible spectrum, are red in color. The rays of shortest wavelength, found at the other end of the visible spectrum, are violet. All the other colors are found between red and violet, and tend to blend into each other. When all the colors are mixed, they appear as white light.

The color of an object depends upon the kind of light the object sends to the eye. This will depend upon the coloring matter or pigments contained in

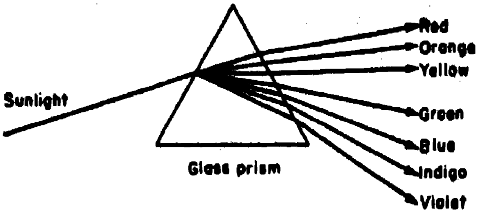


Fig. 27.1.

the object and upon the kind of light falling on the object. If white light falls on a surface, the color of the surface will be determined by those components of the incident light that are reflected and not absorbed or transmitted by the object. For instance, if a surface appears orange in sunlight, it is because the surface has absorbed all wavelengths of sunlight except those in the orange range. If the incident beam of light is not white light, the color of the object will be altered. Thus, if an artificial light beam does not contain some of the color that is reflected from sunlight, the color will appear differently in the two sources of light. If the light source emits light of only a part of the spectrum—as, for example, the yellow light of a sodium flame—then the light beam itself is colored. In fact, any abstraction or loss of part of the spectrum of white light produces a color effect. Some materials reflect one color of light, and transmit a different color.

When a surface absorbs part of the visible spectrum, the color of the reflected light is said to be *complementary* to the absorbed color. The range of wavelengths, color of the corresponding light beam, and complementary colors of the various regions of the spectrum are given in Table 27.1.

TABLE 27.1. ABSORPTION COLORS OF VISIBLE LIGHT

Light Absorbed		
Wavelength, Å	Spectral Color	Complementary Color Observed
4000–4250	Violet	Greenish-yellow
4250–4500	Indigo	Yellow
4500–5100	Blue	Orange
5100–5500	Green	Red
5500–5900	Yellow	Violet
5900–6400	Orange	Blue
6400–7000	Red	Green

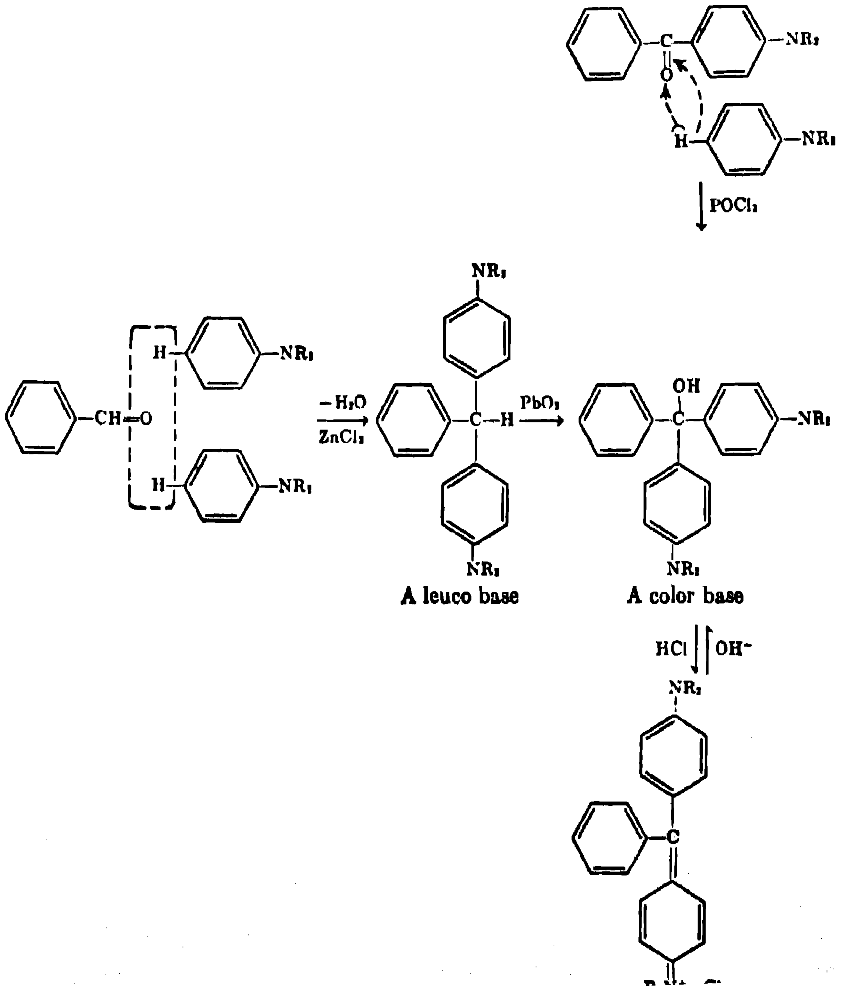
It can be seen that a surface which appears green absorbs light of longest wavelength.

The colors of organic molecules are understood and explained fairly well in terms of the types and positions of chromophores and auxochromes present in a molecule. In general, the more chromophores there are and the longer is the conjugated system in a molecule, the deeper will be its color. This generality is far from being complete. The color of organic compounds, as well as other properties, are more completely accounted for in terms of resonance, steric hindrance, hydrogen bonding, and inductive effects.

27.2 TYPES OF SYNTHETIC DYES

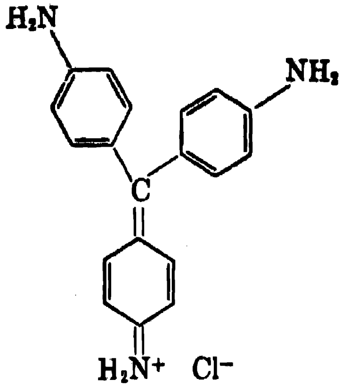
The colorist classifies dyes on a basis of the types of fabrics to which they may be applied, but chemists are more interested in dyes from the standpoint of their molecular structures.

a. Triphenylmethane dyes. Two common routes for the preparation of triphenylmethane dyes are given below (one method starts with a benzalde-

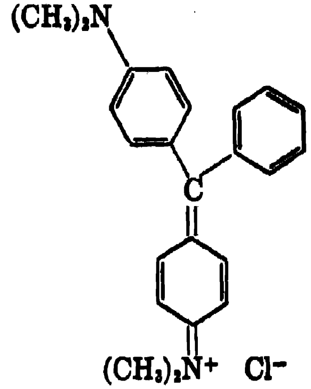


Preparation of triphenylmethane dyes

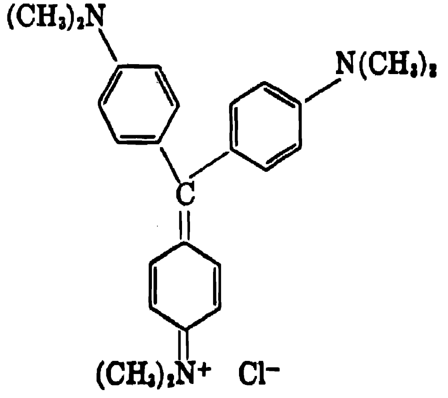
hyde and the other with a benzophenone). The color of the dye depends upon which auxochromes are present. With three —NH_2 groups, one at each *para* position, a red dye results; two —$N(CH_3)_2$ groups give a green dye, and three —$N(CH_3)_2$ groups give a violet dye.



Rosaniline or fuchsin
(red)



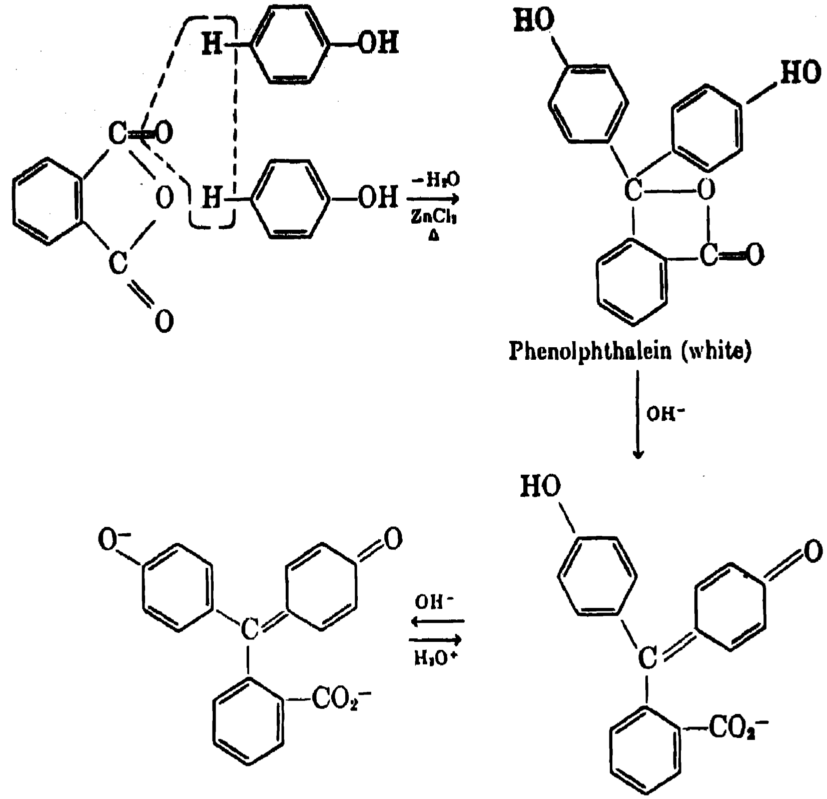
Malachite Green



Crystal Violet

b. Phthalein dyes. Phthalic anhydride condenses with substituted phenols to give products somewhat similar to the triphenylmethane dyes. Phenolphthalein is formed when phenol and phthalic anhydride are fused together with zinc chloride at 200° to 250°. Phenolphthalein is a white, water-insoluble organic compound. Upon the addition of one equivalent of alkali, a monovalent colorless salt is irreversibly formed. The addition of a second equivalent of alkali produces a divalent red salt which may be reverted to the colorless salt upon acidification. This action is the basis for using phenolphthalein as an acid-base indicator: red above $pH = 10$, colorless below $pH = 8$.

Substituted phenols produce other phthaleins. Resorcinol produces fluorescein, named as such because its water solutions show an intense yellow

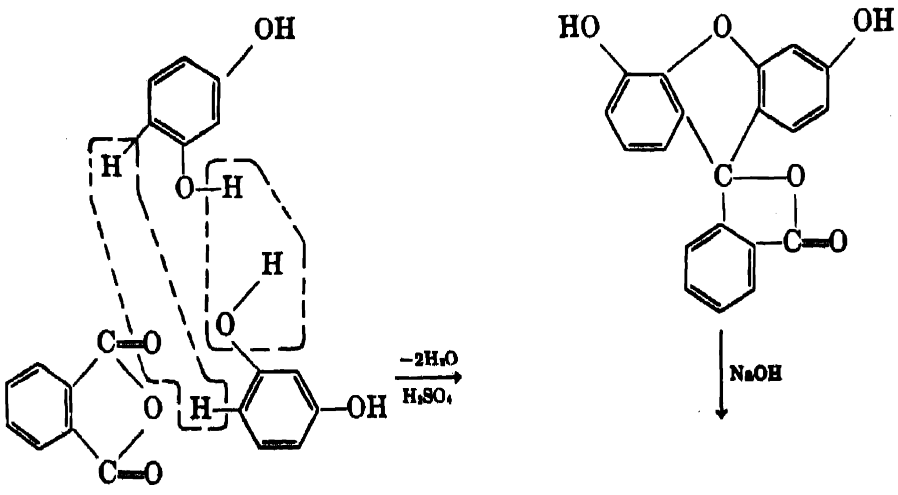


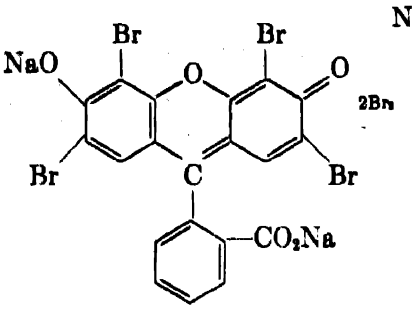
Phenolphthalein (white)

Divalent ion of
phenolphthalein
(red)

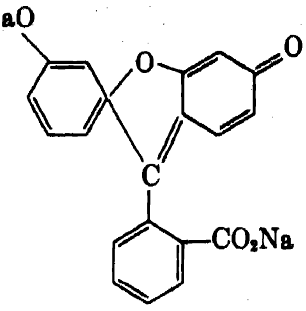
Monovalent ion of
phenolphthalein
(colorless)

fluorescence. Fluorescein is not a good dye, but its tetrabromo derivative is a strong red dye (eosin). (Compare the structure of eosin with that of Mercurochrome, Section 19.3a.)



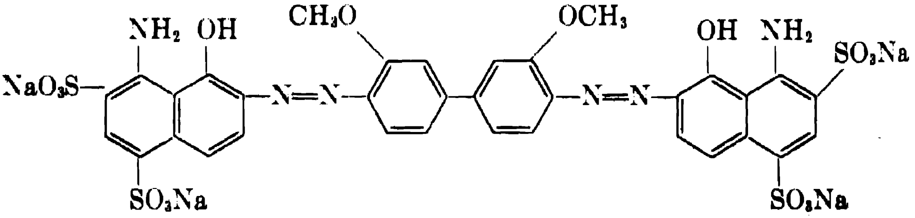


Eosin
(red)



Pale red
with yellow-green
fluorescence

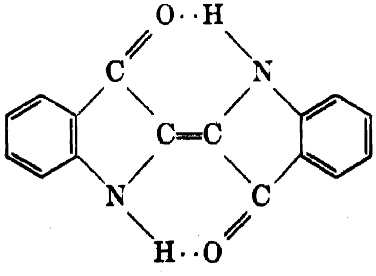
c. **Azo dyes.** One of the most significant events for the dyeing industry was the discovery in 1858 of the diazotization reaction by Peter Griess, who was a student of Kolbe. The coupling of diazonium salts with phenols and anilines in basic solution was discussed in Section 16.1d. Many dyes are prepared by this reaction—dyes that can be used with wool, cotton, acetate rayon, and synthetic fibers, such as Dacron. Most of the dyes contain two or more naphthalene rings, one or two SO_3H groups to render the dyes water soluble, and several OH and NH_2 groups for color variation and fastness. A typical example is Pontamine Sky Blue 6BX, a bright, blue dye.



Pontamine Sky Blue 6BX

d. **Quinoid dyes.** Compounds containing quinoidal rings have colors ranging from yellow to green (across the whole visible spectrum). The best quinoid dyes are derivatives of naphthoquinone and anthraquinone. Quinoid dyes sublime readily and are used for producing colored smokes.

e. **Indigoid and other dyes.** Indigo is one of the earliest natural dyes known to man. Since its synthesis was developed, a number of valuable dyes



Indigo

of similar structure have been produced. The indigoid dyes are noted for their beautiful color effects, durability, and fastness.

Several other types of dyes are used, such as sulfur-containing compounds, cyanine dyes, and carbazole dyes, but the discussion here is limited to those already taken up.

27.3 THE DYEING INDUSTRY

a. Adsorption of dyes on fabrics. To be a dye, a substance must impart color to a fabric, and the color must be stable to light and washing. A permanent dye is said to be a *fast dye*. Not all colored compounds are dyes, because many substances do not adhere to fabrics, or they fade upon exposure to light or washing. Dyes are adsorbed on fabrics by several types of forces, such as ionic bonding, hydrogen bonding, van der Waals forces, chelation, and by solution in the fibers of the fabric. Hence, the applicability of a dye depends upon its structure and upon the nature of the fiber. A striking illustration of the selectivity of fabrics for dyes can be given as follows.[1] Dip a piece of pure cotton fabric and another of acetate rayon into a warm dye bath containing a water-soluble blue dye and a water-insoluble red dye. When the fabrics are withdrawn and rinsed in hot water, the cotton will be colored pure blue, and the acetate rayon will be pure red. On the other hand, the fabrics may be dipped in another pair of dyes, and this time be dyed the opposite colors.

$$\left.\begin{array}{c}\text{Pontamine Sky Blue 6BX}\\+\\\text{Celanthrene Red 3BN}\end{array}\right\}\rightarrow\begin{array}{l}\text{Cotton, dyed blue}\\\\\text{Acetate rayon, dyed red}\end{array}$$

$$\left.\begin{array}{c}\text{Pontamine Fast Scarlet 4BA}\\+\\\text{Celanthrene Pure Blue BRS}\end{array}\right\}\rightarrow\begin{array}{l}\text{Cotton, dyed red}\\\\\text{Acetate rayon, dyed blue}\end{array}$$

Each fabric selectively adsorbs a particular type of dye. The first dye of each pair above is water soluble, and the same hydrogen bonding groups which make it water soluble binds it to cellulose through hydrogen bonds with the cellulose OH groups. Most of these OH groups of cellulose have been covered by acetyl radicals in acetate rayon, which gives it the general characteristics of an ester. Accordingly, it adsorbs dyes which are water insoluble. The mechanism of adsorption in this case is physical adsorption (dipole-dipole and van der Waals forces), or dye molecules may diffuse and dissolve in the fibers. Soaps and detergents are commonly used to help a dye bath wet and penetrate the fabric.

The success of a new textile depends not only upon the suitability of the physical properties of the fiber, but also upon its dyeability. When Orlon and Dacron were first developed, the dyes then available would only impart light tints or pastels to these fibers. This was a serious problem, because no matter how good the fibers were, their markets would have been small if they could not be dyed to bright, deep, fast colors. Several years of fundamental research by Du Pont physical chemists led to a solution of this problem. Similar research by Hercules and other companies was done later for the polypropylene fabrics. Dacron, acetate rayon, and other polyester fibers are generally dyed by nonionic dyes, such as certain quinoid and azo dyes. The dyeing mechanism consists of a dissolution of the dye molecule into the fibers. Orlon is an acrylic fiber whose CN groups form complexes with cuprous ions. Orlon fibers treated with cuprous salts will adsorb anionic dyes. Wool and Nylon being amphoteric, adsorb acidic and basic dyes through ion-pair formation, as well as through hydrogen bonding.

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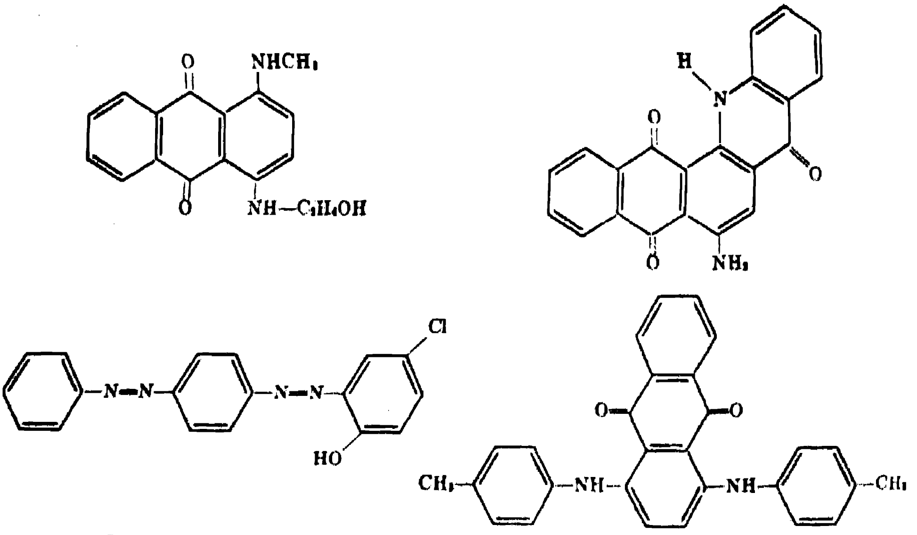
[1] The dyes for these experiments were donated by E. I. du Pont Chemical Company, Wilmington, Delaware.

Another factor important to the applicability of a dye is the correspondence between reactive atoms in the dye and active sites on the fiber. For example, the two dyes below on the left give Dacron a heavy shade, whereas the two on the right are poor dyes for Dacron.



Good dyes for Dacron

Poor dyes for Dacron

b. Methods of dyeing. 1. *Vat dyeing:* In this procedure, a fabric is dipped in a solution of a leuco base (a colorless compound which becomes colored upon oxidation), which gives a color upon exposure to air or chemical oxidation. Many of the indigoid and quinoidal dyes are applied by this method.

2. Mordant dyeing: A fabric is impregnated with a salt by boiling it in a suitable solution, then the fabric is dipped in a dye bath. A chelate is formed involving the dye, the fabric, and the metal ion. This gives the dye superior fastness to light and to washing. Metal ions of iron, aluminum, and particularly chromium are used. Mordant dyes contain acid groups, such as COOH, SO_3H, or phenolic groups, for forming salts with the metal ions.

3. Direct or substantive dyeing: A fabric is dipped in a suspension of a dye of large molecular weight. The dye is adsorbed and held by van der Waals and dipolar forces. This method is used often for polyester fabrics, but seldom for cotton.

4. *Ingrain dyeing:* Azo dyes may be developed right on the fabric by dipping the fabric in a diazonium solution, and then in an alkaline solution of a substituted phenol or aniline. Either order of solutions may be used. This method of dyeing is specially applicable to cotton, because the azo dyes usually have many hydrogen bonding groups present.

c. Dyes from natural sources. Down through history, hundreds of plant and animal sources of coloring matter were known, but as trade between localities and countries increased, only the faster and more brilliant dyestuffs remained in use. In medieval times, the most noteworthy dyes were woad, indigo, logwood, madder, Tyrian purple, kermes, and cochineal.

Woad is a blue dye obtained from the leaves of a plant native to the temperate zone. Eventually it was replaced by indigo.

Indigo was one of the most popular natural dyestuffs. It was obtained from a plant grown chiefly in India and the Far East. It is present as a glucoside in the plant. Hydrolysis yields glucose and a leuco form of indigo. Aeration oxidizes the leuco form, precipitating indigo blue.

Logwood is one of the few natural dyes still used on a commercial scale. It is extracted from the wood of a campeche tree which grows in tropical areas in America. It can be used to dye purple on wool, blue or black on cotton and wool, and purple or black on silk.

Madder was obtained from the roots of the madder plant, grown in most parts of the world. Eventually, it was replaced when alizarin (1,2-dihydroxyanthraquinone), the color component of madder, could be synthesized at a price less than the cost of extraction of madder.

Tyrian purple was obtained from the mucous gland of the purple snail. Before the Fall of Rome, Tyrian purple was used as an emblem of royalty. It is the 6,6′-dibromo derivative of indigo.

Kermes was obtained from a species of louse. It is a brilliant scarlet dye, and replaced Tyrian purple because of a lower cost of production.

Cochineal, also a scarlet dye, is obtained from lice which infest cacti. Its greater brilliance led it to supplant kermes. Then, synthetic azo dyes superseded cochineal, and its use became limited to that of a nonpoisonous food colorant.

Cutch and *fustic* are brownish dyes extracted from acacia and other plants. Various shades of yellow and orange are obtained from different sources. Cutch and fustic are still used today on a small scale.

d. Rise of the synthetic dyeing industry. Today, 99 per cent of the dyeing industry is based on synthetic materials. The beginning of the end of the natural dye industry came in 1856 when William Henry Perkin, at the age of 18, accidentally discovered the azine dye, mauve, while trying to synthesize quinine from crude aniline. He was not the first to synthesize a dyestuff from coal-tar products, but he was the first to realize the industrial possibilities of synthetic dyes, and immediately formed a company to produce the dye.

William Perkin (1838–1907) was studying to be an architect at the City of London School; but, when only 13, he was so fascinated by chemistry that he gave up his lunch periods in order to attend a series of noon lectures on the subject. When he was 15, the famous German chemist August von Hofmann was invited to become the first professor of chemistry at the Royal College of London. Hearing of this, Perkin left his school and prevailed on Hofmann to let him study under him. Under Hofmann, Perkin finished the usual analytical courses in two years and was encouraged to do some research. He was assigned the task of synthesizing quinine from coal tar.

In order to experiment during his spare time on holidays, Perkin fixed up a simple laboratory in his home. During the Easter week of 1856, he was oxidizing some impure aniline oil obtained from coal tar with potassium dichromate. Instead of obtaining white crystals of quinine, he got a black, sticky precipitate. In disgust, he threw it into the sink, and started to clean his tube with methyl alcohol. To his surprise, he got a beautiful purple solution.

Although the practice of that day of just mixing substances together may not be regarded highly scientific, Perkin did his work with care and kept good records. Instead of merely noting the color, and then pouring his purple mixture into the sink, Perkin traced the source of the coloring to an impurity in aniline, namely, toluidine. He obtained a patent and decided to leave college and manufacture the dye commercially. With the financial assistance of his father and the help of his brother who was a builder, Perkin constructed a factory for producing and using his new dye. His product made a hit very quickly, and it was soon a huge financial success. He named the dye "Tyrian purple" after the natural red dye obtained from snails, but it was renamed "mauve" in France, the name by which it is still known.

Perkin's discovery was the stimulus for a big surge of research in organic synthesis. As a result, new dyes and other substances poured from laboratories around the world, particularly those in Germany. Perkin later produced alizarin, which displaced the natural madder.

Perkin, later to be known as Sir William Perkin, received many medals. In 1906, a meeting was held in London to commemorate the 50th anniversary of the founding of the coal-tar industry by Perkin. Emil Fischer came from Germany to present Perkin with the Hofmann medal, Haller from France brought him the Lavoisier medal, and later that year he was invited to the United States to receive the American Chemical Society's first Perkin medal. In 1956, the Perkin Centennial was celebrated in New York City. A distinguished group of European and American experts discussed the economic, social, chemical, psychological, historical, and commercial aspects of color.

One may wonder why Perkin is so well remembered in comparison to others who far surpassed him in brilliance and fundamental scientific discoveries. It is probably because he symbolizes chemical progress through the union of basic and applied research. Perkin's discovery stimulated research in coal tars which led to a vast chemical storehouse. Many diverse commodities are produced from the dye intermediates, such as explosives, perfumes, artificial flavors, anesthetics, solvents, lubricants, inks, lacquers, plastics, and medicinals. Thus, the fabulous coal-tar industry is a boon to mankind, rarely equaled in history.

A good example of how success may depend upon fortuitous timing is the fact that Ferdinand Runge (1794–1867), professor of chemistry at the University of Breslau, was the first to prepare a dye from coal tar (1834), and the first to isolate aniline, phenol, pyrrole, and quinoline from coal tar. The significance of his work was not recognized. This was due, perhaps, to the fact that little was known about coal tar and the structural theory of organic chemistry had not yet been developed.

Shortly after Perkin's discovery, the English made a serious mistake in policy. England and France had rigid patent laws to protect their natural dye products, while Germany had loose patent laws. Also, German researchers and manufacturers received government favor. Consequently, research and industrial production flourished in Germany. Chemists and manufacturers, including scientists of Hofmann's caliber, left England and France for Germany, and soon the German dye industry had a monopoly on the market. Their synthetic methods were patented in foreign countries or held in secrecy. Industries could not get started in other countries because Germany controlled the dye intermediates. In order to prevent internal competition troubles, the six largest German companies formed a cartel, known as the world-famous I. G. Farbenindustrie.

When World War I broke out, panic swept through the Allied countries, because they had been importing 90 per cent of their dyes and intermediates from Germany. Frantic efforts were made to produce dyes, explosives, and drugs from coal tar. One of the first dye manufacturers in this country checked information in two German textbooks and found the reactions so baffling that the first batch of indigo came out yellow-green instead of deep blue.

After the war, the German cartels were temporarily broken, which gave American companies an opportunity to get started. This changed the competitive status of the industry. Dyes are still imported chiefly from Germany and Switzerland, but the major portion of dyes used in the United States are American-made pigments. In 1955, 36 per cent of all dyes made were azo dyes, 24 per cent were anthraquinone vat dyes, and 9 per cent were indigoid dyes. Modern-day materials can have as many as 70,000 shades. One company alone makes over 800 different dyes, offering the customer a choice, for instance, of more than 120 reds, 50 yellows, 145 blues, and 70 browns. Synthetic dyes have done what natural dyes failed to do, namely, give bright, fast colors to plastics and synthetic textiles.

27.4 OTHER USES OF DYES

Dyes are used in several ways other than for dyeing fabrics. They serve as indicators for the control of chemical processes and are used for staining biological substances, printing inks, color photography, and medicinals. A number of dyes have been used at times for certain physiological actions. For example, phenolphthalein is an extremely powerful laxative, Salvarsan (Arsphenamine, in this country) is used to treat syphilis, and Prontosil (page 607) has been used against infectious diseases.

STUDY EXERCISES AND PROBLEMS

1. Describe the visible spectrum.

2. What is the relationship between the colors of the spectrum and their complementary colors?

3. What interaction or physical process occurs in molecules when they absorb light energy in the visible and ultraviolet regions of the spectrum?

4. What are chromophores and auxochromes?

5. Which compound in the following pairs would be expected to have the deeper color, and on what basis do you make your decision? (a) $C_6H_5—CH═N—N═CH—C_6H_5$ or $C_6H_5—CH═N—CH_2CH_2—N═CH—C_6H_5$. (b) *p*-Nitrochlorobenzene or *p*-nitroaniline.

6. Explain the fact that, although a buna S rubber molecule has thousands of C═C bonds and phenyl groups, it is colorless, while $\phi—CH═CH—CH═CH—CH═CH—CH═CH—\phi$ is yellow.

7. What volume of 10 *N* HCl would be required to convert 17.3 g of the color base of Malachite Green to its salt?

8. If one diazotizes 17.3 g of sulfanilic acid in hydrochloric acid with an assumed yield of 80%, and to this he adds 12.1 g of N,N-dimethylaniline, what weight of dye can he expect to obtain if the coupling reaction takes place with an 80% yield?

9. By what types of forces are dyes bonded to fabrics?

10. Describe the methods of (a) vat dyeing, (b) mordant dyeing, (c) ingrain dyeing, (d) substantive dyeing.

11. Name three dyes formerly or at present obtained from natural sources.

12. What is the significance of Sir William Perkin's discovery?

13. Why did Germany have a monopoly on the coal-tar industry in 1914?

14. In what ways are dyes used other than for dyeing fabrics?

15. Give the structure of one member of each of the following types of dyes: triphenylmethane, azo, indigoid, phthalein, and quinoid.

16. A chemist prepared a dye bath for ingrain dyeing and forgot how much naphthylamine he had put in solution. How would you proceed to find out how much naphthylamine was in the dye bath? What quantity of chemicals would be required or produced, depending on your method of analysis, if the solution contained 14.3 g of naphthylamine per liter of solution?

17. With benzene as the only aromatic compound available, how can Malachite Green be prepared in the laboratory?

18. The structures of the red and colorless forms of phenolphthalein are given on page 597. How do you account for the difference in color of the two forms? On this basis would you predict phenolphthalein to be red in concentrated sulfuric acid?

28

Chemotherapy

The practice of medicine has been revolutionized by the phenomenal success of certain drugs, notably the sulfa drugs, antibiotics, steroidal hormones, and, most recently, the psychochemicals. Most present-day prescriptions call for one or more of these miracle drugs. It is interesting that 90 per cent of the prescriptions written today could not have been filled in 1935 because the prescribed drugs were unknown or commercially unavailable at that time.

Infectious diseases are caused by certain agents foreign to our bodies usually given the unspecific terms *germs* or *microbes*. These microorganisms are of three types—bacteria, protozoa, and viruses. Bacteria are minute forms of plant life and produce such diseases as pneumonia, tuberculosis, diphtheria, and cholera. Protozoa are microbes of animal nature, causing such diseases as malaria, syphilis, and dysentery. Viruses are high-molecular-weight proteinic substances with the ability to reproduce when in proper environments. They produce such illnesses as measles, influenza, smallpox, polio, and the common cold. It is believed that the systems of microbes and mammals have the same basic type of metabolic processes. When a drug is administered, it probably interferes or ties up some substance indispensable to the disease germ, but not to the host. Thereby, the germ is killed, and the symptoms of illness disappear. This is the essence of chemotherapy. In addition, some ailments such as aging, hardening of the arteries, arthritis, and mental disorders are not caused by germs. Medical treatment has progressed much slower in this direction, but recent advances offer promise for the near future.

28.1 GENERAL DESCRIPTION

Chemotherapy may be defined as the use of chemical agents for the selective destruction of parasitic organisms within a host. The objective is to destroy the invading organisms without doing harm to the normal cells of the host. The practice of chemotherapy has two stages. One is the determination of the structure of active agents in medicinals obtained from natural sources. A second phase consists of making minor modifications of the natural drug structure and correlating biological activity with chemical structure until a compound of optimum effect can be prepared.

An excellent example of the first stage of chemotherapy is found in a World War II project. Recognition of the potential military importance of penicillin in the early 1940s led to a vast, restricted, international, experimental and theoretical investigation of its chemical structure and methods for its commercial production. Thirty-nine American and British scientific groups collaborated on this project. It took about three years of intensive, cooperative work to learn the chemical structure of penicillin and to produce it economically for commercial use.

The second stage of chemotherapy is illustrated by the search for an antimalarial substitute for quinine. Shortly after Pearl Harbor, 90 per cent of the world's supply of quinine—the standard antimalarial—fell into the hands of Japan. From 1941 to 1945, an extensive search and testing program was carried on at about thirty universities and several government and industrial laboratories. There were prepared and tested almost 15,000 compounds, among which one or two good antimalarials were found.

Another equally successful application of this second stage of chemotherapy was the development of the analgesic, *phenazocine*, by E. L. May and coworkers at the National Institutes of Health. About 70 compounds related to morphine with various functional group and position alterations were synthesized and tested for their analgesic effect in mice. Promising compounds were then tested at the University of Michigan for their ability to suppress withdrawal symptoms in monkeys addicted to morphine. These tests were followed for toxicity in various animals for periods of about three months. Compounds which still showed promise were tested exhaustively for their analgesic effects in man at the Public Health Addiction Research Center. The physiological and psychological addiction characteristics were determined in former drug addicts for six to nine months. Out of these tests, phenazocine proved to be better than morphine by being 5–10 times as potent and of lower toxicity and addicting properties. It is particularly effective in cases of extremely severe pain and offers the additional advantage of being capable of synthesis on a commercial scale.

These examples illustrate the general approach of chemotherapy. Now it is being applied to the cancer problem. A vast screening program is being administered by the United States Public Health Service to find substances that will retard or stop the growth of cancer cells. In 1961 alone, 50,000 substances were screened and about 175 drugs were in various stages of clinical tests.

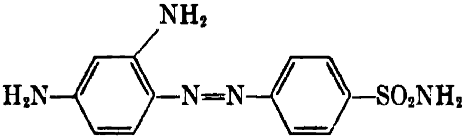
28.2 THE WONDER DRUGS

The impact which the sulfa drugs and later members of the so-called wonder drugs have made upon life can be vividly shown by two incidents which happened a dozen years apart. In 1924, the son of President Calvin Coolidge blistered his heel while playing tennis, blood poisoning set in, and he died. In 1936, the son of President Roosevelt suffered a sinus infection. He was given a sulfa drug, his temperature dropped within hours, and he recovered. Thus, the dozen years that separated these two events marked a new era in medicine.

Thanks to modern practices of medicine and surgery, and particularly to the action of the wonder drugs, our health is better and we live longer. The formerly feared diseases, smallpox, diphtheria, lockjaw, blood poisoning, and others are almost obsolete now. Rarely do we see a quarantine sign. As late as the 1930s, pneumonia killed most of those it attacked. Today, a physician is reluctant to admit he has lost a patient to pneumonia. Within one generation the wonder drugs have reduced fatalities from scarlet fever by 96 per cent, from diphtheria by 96 per cent, from whooping cough by 97 per cent, and from polio by 95 per cent. An interesting paradox is that over the last 15 years the life expectancy of the average American has been rising at the approximate rate of a half-year each year. At this rate, each year that we live we can expect to live half a year longer, or in other words, each year we use up only half a year of our lives.

a. The sulfa drugs. The sulfa drugs are derivatives of sulfanilamide, $H_2N—C_6H_4—SO_2NH_2$. They were the first compounds found effective against the types of bacteria that produce tuberculosis, pneumonia, and diphtheria.

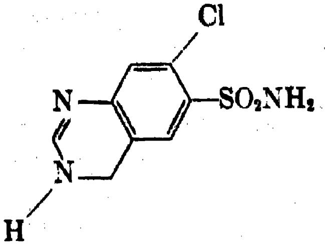
In the early 1930s, Gerhard Domagk was testing certain dyes for their effect on germs in mice. His daughter pricked her finger with a needle and infection set in. All attempts, even surgery, failed to stop the spread of deadly infection. Domagk, in desperation, gave his little girl oral doses of one of his dyes being tested. Her fever dropped quickly, and she recovered. Domagk had previously discovered that the dye, patented under the name of Prontosil, would cure infected mice and rabbits with no apparent harm to the animals.



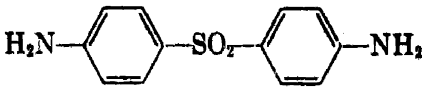
Prontosil

The work of Domagk and his co-workers attracted many followers. Two French scientists soon learned that Prontosil is degraded *in vivo* to sulfanilamide and that this is the active portion of the Prontosil molecule. In a few years, many derivatives of sulfanilamide were prepared and tested, the number reaching over 1300. As a tribute to his pioneering work in the field, Domagk was selected for the 1939 Nobel Prize in Physiology and Medicine, but Hitler prohibited Domagk from accepting it.

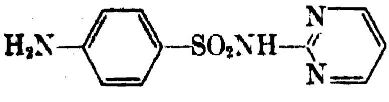
Although other classes of compounds are active against bacteria, such as p-nitrobenzoic acid, arsenic compounds, and sulfones, the sulfanilamides are the most effective compounds with little toxicity. Several types of bacteria were found susceptible to sulfanilamide. Pneumonia, gonorrhea, some types of meningitis, blood poisoning, scarlet fever, tonsillitis, and sinus infection are just a few of the many that have been treated successfully:



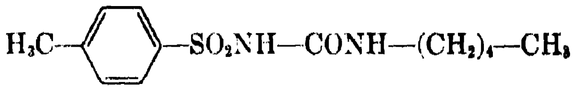
Chlorothiazide
(important class of diuretics[1])



p,p′-Sulfonyldianiline
(treatment of choice for leprosy)



Sulfadiazine
(for meningococcal meningitis)



Tolbutamide
(for diabetes)

b. Antibiotics. Not all microbes are harmful. Man could not survive if it were not for certain microbes. There are microbes which decompose noxious wastes into harmless chemicals and return them to the earth. There are microbes in the mouth and respiratory tract that protect against infection, and microbes in the colons that produce vitamins. Alcohol and cheeses are the products of microbic processes.

Just when it was becoming more evident that there are some germs resistant to the sulfa drugs, the potentiality of antibiotics was discovered. The term *antibiotic* means "against life." Antibiotics are substances, produced by microorganisms, which inhibit the growth or destroy other microorganisms.

The discovery and rise of antibiotics is an interesting tale. A British bacteriologist, Alexander Fleming, had been cultivating various bacteria in dishes. One morning in 1928 Fleming noticed that the bacteria in one dish were normal except within a ring of blue-green mold, where the germs had all died. Fleming cultivated the mold, from which he got a broth. He found this solution, which he referred to as penicillin, to be very effective against pneumonia germs in mice, and in 1929 he published his results.

Fleming's article received little attention until about ten years later. Aware of the success of the sulfas and inspired by Fleming's article, Florey and Chain at Oxford University set out to obtain a concentrated batch of Fleming's penicillin to try on human beings. After three years of hard work, they obtained a few grams of a brownish powder.

On February 12, 1941, the first dose of penicillin was given to a human patient. A policeman in London nicked himself while shaving and got a blood infection. His face became covered with abscesses and he had a burning fever. Sulfa drugs were tried, with no success. An injection of penicillin was given to the dying man, and his temperature dropped abruptly. He was on the road to recovery when the supply of penicillin ran out. The infection flared up again and the patient died.

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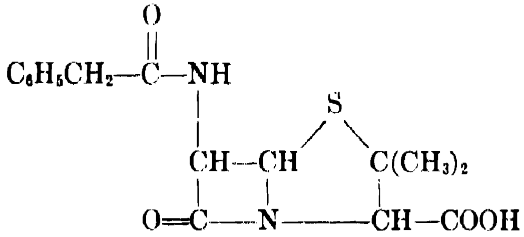
[1] A *diuretic* is an agent used to increase the volume of urine.

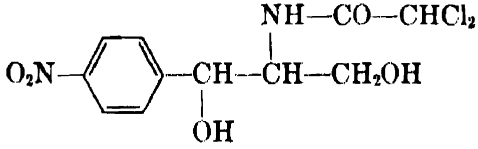
Some months later, another batch of penicillin was tried on a boy with a strep infection that did not respond to any other treatment. The boy recovered, and the power of penicillin was proved.

At the time, England was at war. Aware of the potential military value of penicillin, Florey came to the United States to seek financial and physical aid for its production. As stated before, a vast research program was set up between Canada, England, and the United States to find methods for mass production of penicillin and to learn its chemical structure for possible synthesis. Although it can be synthesized now, it is still produced in large fermentation tanks.

Penicillin is obtained from the mold commonly found on stale bread, cheese, or fruit. It proved to be very effective against pneumonia, scarlet fever, wound infections, gonorrhea, syphilis, and many other diseases. However, it is not effective against tuberculosis. Fortunately, other antibiotics were found that may be used against tuberculosis, most notably, streptomycin.



Benzyl penicillin



Chloromycetin

At the time Florey was attempting to produce penicillin, Rene Dubos in the United States isolated an antibiotic from a bacterium. The antibiotic tyrothricin was too toxic for injection, although it could be used on surface wounds. Dubos' work attracted a former teacher and associate of his, Selman Waksman. Waksman had been studying soil microbes for many years. Dubos' success with tyrothricin prompted Waksman to examine his soil microorganisms for useful antibiotics. He and his assistants screened more than 10,000 soil cultures, among which 100 had possibilities. Ten of these were worthy of intensive study, and one of these, streptomycin, turned out to be highly valuable. This discovery was made in 1944, the year penicillin went into mass production.

Streptomycin is particularly effective against tuberculosis, kidney infections, and a deadly form of pneumonia. The success of streptomycin spurred an extensive search for other antibiotics from soils all over the earth. It was like hunting for gold—antibiotics were where you found them. We can see now some merit in the early practices of the Greeks who used warm soil, of the English medievals who used molded bread, and of the ancient Chinese who used bean curds to promote healing of wounds. Soon after streptomycin, there were found chloromycin, aureomycin, terramycin, and many others. Each had to go through an intensive testing program. Those which may be used for several ailments are referred to as *broad spectrum* antibiotics. There is considerable overlapping among them, but each is usually superior against some specific disease.

Antibiotics are not effective against viruses. Collectively, the sulfas and antibiotics have markedly changed public health. For illustration, compare the situations before and after the appearance of these wonder drugs. The decade 1935–1945 witnessed the most significant advance in medicine and public health in history.

Disease	*Before 1935*	*After 1945*
Skin and blood infections	Probable loss of limb or life	High probability of quick elimination
Pneumonia and tuberculosis	Among top killers	Rarely fatal
Mastoid ear infections	Common, and usually cause deafness	Uncommon
Syphilis and gonorrhea	Prevalent	Quickly cured
Endocarditis (inflammation of heart valves)	100% fatal	Over 60% of the cases recover
Meningitis	Almost always fatal	Frequently curable
Cholera, typhoid fever, and diphtheria	Usually fatal	Usually cured

In general, the effect of chemotherapy upon public health in the United States has been to retire the infectious diseases as leading causes of death and make chronic diseases attending old age the major health problems. Thus, pneumonia and influenza combined were the second-ranking causes of death in 1930 but were ranked sixth in 1960, and the patient's chances for survival had risen from 3 to 1 in 1935 to more than 12 to 1 in 1956. It is estimated that chemotherapy saved 1,100,000 lives in cases of pneumonia and influenza alone in the 15-year period 1938 to 1952. Tuberculosis was the second-ranking cause of death in 1900 and by 1954 was no longer on the list of the ten leading causes of death. Syphilis has retreated to the point where some cities are considering abandoning the premarital testing program. Smallpox killed 60 million Europeans in the 18th century but is nearly nonexistent in the United States today.

In contrast to these triumphs, cancer ranked eighth in 1900 as a leading cause of death and has ranked second since 1940. Heart disease ranked fourth in 1900 but is now first. The major causes of death in the United States in 1960 ranked as follows:

1st—Diseases of heart and blood vessels
2nd—Cancer
3rd—Vascular lesions affecting nervous system (chiefly strokes)
4th—Accidents
5th—Certain diseases of early infancy
6th—Influenza and pneumonia

Until major progress is made, 1 out of 10 persons in the United States will be hospitalized for mental illness, 1 out of 4 persons will be treated for cancer, and 1 out of every 2 persons can expect to die of cardiovascular diseases. In Asia, where there is a lower standard of living, the top killers are epidemic diseases such as tuberculosis, beriberi, malaria, yaws, and pneumonia.

Antibiotics are not limited to medical usage. The addition of antibiotics to the feed of livestock hastens their growth so that they can be shipped to market in 10 to 25 per cent less time. This saves millions of dollars in feed and keep. In spite of all present preservation measures, one pound of food out of every four pounds spoils. Antibiotics retard spoilage, saving millions of dollars, especially in countries with limited refrigeration.

c. Hormones and vitamins. It was stated in Section 22.6a that all biological processes are catalyzed by enzymes and that enzymes are complex protein molecules. Many enzymes need to be activated by vitamins or hormones. In fact, most vitamins and hormones are enzyme activators, although some may serve as direct catalysts for biological reactions. Some hormones are proteins, some are steroids, and a few are large amino acids. Some vitamins are proteins, whereas others are ordinary organic compounds. The only essential difference between hormones and vitamins is that the former are manufactured in glands, whereas vitamins are obtained from our food. Hence, they are both catalysts, found in our bodies in very small amounts. The amount of female hormones secreted by an adult woman in six months weighs about the same as a postage stamp.

Hormones and vitamins activate or deactivate certain enzymes which, in turn, regulate certain organs and processes in our bodies. Consequently, hormones and vitamins have a strong influence on our physical and mental health. For instance, the thyroid gland produces a hormone that contains iodine and governs the rate at which the body produces energy. The pancreas produces the proteinic hormone insulin, which regulates the burning of carbohydrates as a source of energy. Adrenalin from the adrenal glands affects nerves controlling involuntary muscles, which permits us to put forth a sudden burst of action. The effects of vitamin deficiencies are quite familiar. Vitamin A is necessary for seeing in dim light, vitamin D for proper bone formation, vitamin C for keeping blood vessels strong, vitamin K for clotting of blood, and vitamin B for blood formation and other processes. The administration of certain hormones and vitamins has marked effects on our health, and they are used in the treatment of more than thirty diseases.

The falling death rate and the consequent increase in the number of elderly persons in the United States have resulted in an increased incidence of arthritis. Twenty-five years ago there were scarcely any arthritis clinics; today there are hundreds. Among the four chronic forms of arthritis, rheumatoid arthritis is probably the most prevalent. The steroid cortisone has been very effective in relieving patients of the painful symptoms of rheumatoid arthritis. The same effects are obtained with ACTH, which stimulates the adrenal gland to release cortisone.

The initial commercial source of ACTH was the tiny pituitary gland of hogs, but it takes at least half a dozen of them to yield an average medical dose. More recently, manufacturers have used the pituitary gland of whales, which is about the size of a chicken egg.

Hormones sometimes do not kill the germs but only banish the symptoms, and the infection continues to grow. Since the discovery of cortisone and ACTH for arthritis, these hormones have found valuable applications in rheumatic fever, bronchial asthma, skin diseases, and other inflammatory disorders. Because of the frequent unpleasant side effects of cortisone, it has been largely supplanted by hydrocortisone and other steroids.

d. Psychochemicals. About 160 years ago the French physician Philippe Pinel risked his life to change the treatment of the insane from confinement in prisons to medical care. Now, another revolution in the treatment of mental cases is taking place. With the aid of psychochemicals—substances which induce behavioral changes—psychiatrists can (1) stop some outbreaks of emotional illness at an early stage, (2) treat current cases more effectively, and (3) make "hopeless" cases accessible to therapy by reducing their anxiety and removing the barriers between patient and psychiatrist. For the first time, the upward trend in mental hospital cases was reversed in 1956. It is significant that the number of admissions has increased but the number of patients discharged has increased at a faster rate. Still, half of all patients in hospitals are mental cases.

Like the antibiotics and the sulfa drugs before them, the psychochemicals have had a spectacular meteoric rise. Thirty per cent of all prescriptions written today contain some psychochemicals. The Indian biochemists Sen and Bose first reported the effect of Rauwolfia extracts on high blood pressure and various "manias" in 1931, but the active alkaloid, reserpine, was not isolated until 1952. Since then, a score of alkaloids and synthetic drugs have invaded the market. Essentially, the drugs are tranquilizers (ataraxics); they do not cure, but they make the patient receptive to treatment of the underlying disease. One significant aspect of these drugs is that they indicate mental illness has a chemical basis and can be countered chemically.

Some early results are extremely encouraging. When injected with chlorpromazine, persons who had been maniacs for a year or more—patients who try to assault doctors and are admitted to hospitals "swinging from chandeliers that are not there"—soon quieted down and were content to lie down on their beds. They remained calm, fed themselves, ate heartily, and slept well. Among 77 patients, 37 went home for home treatment, and 27 improved somewhat.

A different group of patients, in whom all approved treatments had failed to bring lasting improvement, were given reserpine and the normal psychiatric help. Among 82 patients, 59 were discharged, 12 showed varying degrees of improvement, and 11 were unchanged.

In a five-year study with 250 mentally retarded children—ranging from destructioners and breath-holders to vomiters, teeth grinders, and head bangers—chlorpromazine was effective in relieving most of the symptoms in 40–80% of the cases.

There are about 300,000 schizophrenics in U.S. mental hospitals, and after a stay of two years or so, their chances of being discharged are very slim. The new drugs have already changed this situation. A new mental patient entering the hospital in 1932 could expect to spend 30 years or life there. Today, about two out of three of all new admissions are discharged in one year or sooner.

The drugs are used with a wide variety of patients. They quell the bickering of senile patients, delirium tremens in patients subside abruptly, the agonizing symptoms of withdrawal from narcotics—nausea, retching, chills, and weeping—are banished, and excited patients surrender meekly to medical or surgical treatment.

As one can expect, not all patients respond, and there are some serious, undesirable side effects. About 5% get a form of jaundice, some acquire stooped postures and wooden facial expressions, and most suffer a decline in blood pressure. The most serious drawback of reserpine is that it induces mental depressions so severe that some patients have committed suicide. The latest formulations contain a substance added to counteract the depressing effect of reserpine without impairing its tranquilizing effect. Efforts to develop new antidepressants are as great as those in search of new tranquilizers. There are thousands of people plagued by a brooding sense of despair, guilt, fear, and insomnia.

Indoklon, hexafluorodiethyl ether, has recently been approved by the Food and Drug Administration to replace electric shock therapy in treatment of acute depression. Indoklon eliminates some of the undesirable side effects related to shock treatments and can be taken by patients who fear electric shocks.

Serotonin, a hormone-like compound, is present in the brain, and an excess of it can block the "nerve switchboards" in the brain and other parts of the central nervous system. An imbalance of serotonin may cause a mental disorder. It is believed that tranquilizing drugs affect the concentration of serotonin and other hormones in the central nervous system, but it is not completely clear how this is done. Several laboratories have started intensive studies on brain chemistry.

The much-discussed population explosion has stimulated activity among many drug firms to find a cheap, oral contraceptive. The present world population, some 3 billion, is double that of 70 years ago and forecasts call for this number to double within 40 years. Unfortunately, the greatest growth is in poorer, less developed regions. Hope of slowing the population increase through drugs rose when in 1956 oral antifertility agents were found to stop ovulation. Most drug firms now are exploring a wide variety of substances to find an agent which is 100 per cent effective and has few side effects. Frequent side effects observed so far include nausea, midcycle bleeding, breast tenderness, and weight gain.

28.3 MECHANISM OF DRUG ACTION

In spite of the remarkable progress in chemotherapy, scientists are still in the trial-and-error stage of finding new drugs. One cannot sit down and plan the structure of a compound which would have a certain desired physiological activity. Only by testing compounds of various structures are new ones of partial suitability discovered. A slight alteration in the structure of a compound frequently nullifies its action completely or, with continual use, undesirable side effects may develop to prohibit its use.

The situation is that the body is a highly organized, delicately balanced, dynamic system of physicochemical equilibria. Illness is an indication that some one or more equilibria in the total system have been disturbed. By medical treatment the physician may partially rebalance these equilibria, or by surgery the surgeon may even bypass them, only to learn later that this has upset some other part of the complex network of interrelated equilibria. For instance, it was learned that 2,4-dinitrophenol interferes with the normal metabolism and causes the consumption of foodstuffs to be dissipated as heat rather than stored up as fat. This led to prevalent use a few decades ago of

2,4-dinitrophenol as a reducing agent, until several cases of cataract were traced back to its use. Thus, a disturbance in one place of the body's balanced network of equilibria may cause an undesired upset in some other remotely connected part of the system. Much more needs to be learned about the steady state of this intricate system.

This is extremely difficult to do, because any alteration of one part of the system causes a change and readjustment of many other parts of the system. A chemist can study the over-all metabolism of an organism—what goes in, what is present at any particular time, and what comes out—but rarely has it been possible to unravel the details of the intermediate steps. A crude analogy of the situation has been given as follows. Imagine a factory in operation. A chemist on the outside could examine the in-going raw materials and the products coming out, and he could look through the windows to study some of the activities inside. But, there is much he cannot learn by merely looking in from the outside. Much goes on behind solid walls beyond his vision. He might break in to examine what goes on in any given room, but then the occupants may leave or stop working, and their relations with the rest of the plant may cease.

In a similar fashion, chemists have been attempting for years to learn the mechanisms of biological processes. The advent of certain techniques since World War II has made possible tremendous progress in this direction. For example, the process of photosynthesis has been known for more than one hundred years, by which process the living cell transforms carbon dioxide and water into sugars in the presence of sunlight and chlorophyll. For almost ninety years, many unsuccessful studies were made to learn the sequence of reactions by which the carbon dioxide is converted into sugars. Many proposals were made, but these were hardly more than guesses, for it was like trying to tell from the outside what goes on in a closed box. Then, just after the war there was the coincidental development of three powerful tools, and fortunately a group of scientists recognized their usefulness for attacking this problem. Thus, in order to determine the path of carbon in photosynthesis, Calvin and his co-workers at the University of California used radioactive carbon-14, obtainable from the pile at Oak Ridge; they used paper chromatography, first developed by the British Nobel Prize winners Martin and Synge; and they used autoradiography. As a result, they learned the sequence of reactions and compounds formed by which CO_2 is converted into carbohydrates.

When a drug is taken, it may have to pass through several physicochemical stages before it reaches its site of action. Thus, it may have to diffuse through membranes, pass from lipoid to aqueous or aqueous to lipoid phases, suffer degradation, or form weak complexes for penetration of cell walls. Any one of these steps may be the critical step, and if a physical process is the significant step, a correlation between drug action and the physical property may be observed. For example, the anesthetic potency of most active agents have been correlated with oil-water distribution coefficients, the ability to lower water surface tension, and the vapor pressure of their clathrate hydrates. This has led to some speculation about their mechanism of action, but still no proved theory has been established. At the cellular level, generalizations have been found relating biological activity to membrane permeability, basicity, complex-forming ability, dissociation constants and *p*H, and thermodynamic activity. A vast amount of attention has been given also to relationships between the chemical constitution of a substance and its biological activity. A number of correlations have been found, referred to as structure activity relationships (SAR), but all are limited and frequently have exceptions. A unified theory of drug action is far from being realized. One scheme by which more and more SAR success is being achieved is by studying the spatial shape of molecules. For example, it has been shown that the structures of several substances having morphine-like action are quite different when drawn on a plane. In the three-dimensional structures of the compounds, however, there can be found the same N-methylpiperidine system. In another example, it is possible to relate the insecticidal activities of a number of compounds (DDT, benzenehexachloride, their analogs, etc.) to their abilities to fit into a certain-shaped cavity.[2] In another example, it has been found that the intensity of action of common parasympathetic stimulants is related to the size of the cationic head and the length of the group R in molecules of the type R—G$^+$. The most powerful drugs have five atoms in R, and the size of G$^+$ is close to that of —$N^+(CH_3)_3$.[3] It has been possible to classify the odor of hundreds of compounds on a basis of their having molecular shapes corresponding to one or more of seven primary odor receptor sites.[4] For instance, "globular" molecules like camphor, benzenehexachloride, hexachloroethane, and durene (1,2,4,5-tetramethylbenzene) have a camphoraceous odor.

The SAR idea was first expressed by Paul Ehrlich more than a century ago under his lock-and-key theory. It is now generally believed that drug action in most instances depends upon activation of receptors located in the surface of a cell. This surface may be regarded as a mosaic of "keyholes" formed by enzyme and other biological constituent molecules. Foreign molecules of the right size and polar distribution fit the keyholes selectively like a key fits a lock. However, other molecules of similar shape, but useless physiologically, may also partially fit a given keyhole. The molecule then blocks the entrance of a biologically active molecule. This may have an adverse effect (toxic) or a beneficial effect (medication), depending upon the nature of the molecules involved. This is the principle of *competitive inhibition* first demonstrated by

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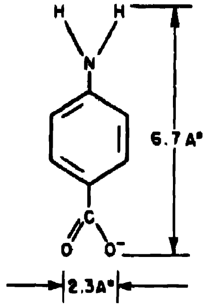
[2] L. J. Mullins, *ibid.* **122**, 118 (1955); R. W. Hummer and E. E. Konaga, *ibid.* **113**, 653 (1951).

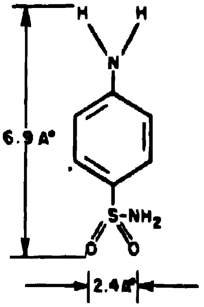
[3] H. R. Ing, *ibid.* **109**, 264 (1949).

[4] J. E. Amoore, J. W. Johnston, Jr., and M. Rubin, *Scientific American*, Feb. 1964, p. 2–9.

Quastel and Woolridge in 1928. For example, *p*-aminobenzoic acid, a part of a vitamin B molecule, is necessary for the survival of certain bacteria. Owing to the resemblance in size and electron pattern of *p*-aminobenzoic acid and sulfanilamide, the latter compound may fit into the enzyme surface normally reserved for *p*-aminobenzoic acid. This may block the metabolism of a disease germ, and it will die; thereby sulfanilamide exhibits drug activity. This explains why antibiotics are ineffective against viruses. Antibiotics work by inhibiting some key enzyme, but viruses have no enzymes of their own. They use enzymes of the host.

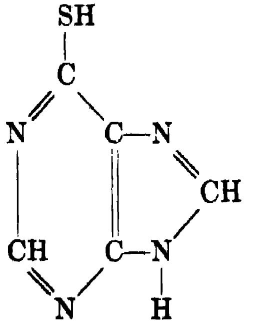


p-Aminobenzoate ion

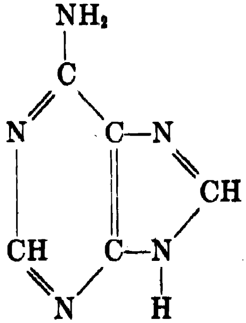


Sulfanilamide

After Woods revived the principle of competitive inhibition in 1940, an extensive search was made in many laboratories for antagonists of known metabolites (antimetabolites). Within a few years, antimetabolites were known for most water-soluble vitamins and for many hormones and amino acids. This knowledge was of tremendous aid in designing the structure of new potential drugs. For one example, 6-mercaptopurine is an analogue of the nucleic acid constituent adenine (page 529). As an antimetabolite of adenine, 6-mercaptopurine interferes with nucleic acid synthesis and has proved to produce a significant partial or complete remission of leukemia.



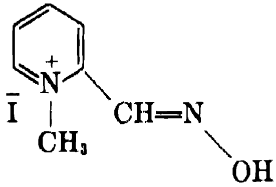
6-Mercaptopurine



Adenine

It is not necessary for the whole molecule of a metabolite or antimetabolite to fit the receptor site of the cell. Only a certain "active portion" must fit the major portion of the receptor site. The rest of the molecule may affect the shape of the active moiety, and thereby partially determine the degree of complementariness of the lock-and-key coupling. This may modify the rate or intensity of response for a given compound. Use of homologous series of compounds has furnished information on the dimensions of active sites. In any event, it can be seen that this lock-and-key view may be applied to a wide variety of biological responses. Keep in mind that this principle implies that a molecule must also have the proper pattern of electron densities arising from formal charges, electronegative atoms, etc. For example, the nerve stimulating activity of choline esters and ethers is directly related to the electron density on the ether oxygen atom.

A good illustration of the application of this lock-and-key concept for finding a drug is provided by the development of a drug to repair the lesion produced by nerve gases. It was found that the enzyme cholinesterase controls hydrolysis of acetylcholine which is involved in transmission of nerve impulses. Nerve gases get their lethal punch by damaging cholinesterase, thereby blocking vital nervous activity. Years of research led Nachmansohn and Wilson to the notion that a good antidote would be a hydroxylamine derivative with a positive charge at a specific distance from the N—OH group. Such a compound, PAM, was designed, prepared, tested, and found to be 100 per cent effective against certain toxic nerve gases and insecticides.



PAM
2-Pyridine aldoxime methiodide

Two major problems facing chemotherapists are side effects and development of drug resistance. No drug is completely free of producing undesirable side effects, although these side effects are sometimes negligible. Even aspirin cannot be taken by all persons without some unpleasantness. Penicillin normally has a low toxicity, yet there are patients who are allergic to it. In fact, over twenty different types of side effects have been observed with penicillin treatment. It is not uncommon for streptomycin to produce dizziness, ringing in the ears, or even impairment of hearing. Reserpine often aggravates peptic ulcers or may cause severe depression and suicidal impulses, and other tranquilizers may produce severe convulsions, an arched stiff back, or eye rolling. Administration of hormones or anesthetics to pregnant women may produce defected babies, and one of the worst was *Thalidomide* which was believed to be responsible for the birth of thousands of mongoloid babies. Many side effects are less common now, because doctors are more watchful for such events. Side effects arise from drugs because of individual metabolic differences. Hence, a drug is usually effective for no more than a large majority of the population.

Frequently, a disease may be successfully treated by a particular drug, but after a given period, the drug loses its effectiveness. There are several theories, but it is not known conclusively why bacteria acquire this drug resistance. One method of diminishing this effect is to administer large doses in order to kill as many germs as possible in the first treatment. The fewer the surviving germs, the slower are drug-resistant strains produced. Of course, too large a dose may be toxic. Proper dosage is important. Also, mixtures of antibiotics and sulfa drugs are administered to retard development of drug resistance. Nevertheless, a ceaseless search for new drugs must be made to supplant those which drug resistance has made almost useless.

28.4 SUMMARY

This chapter has not attempted to give the structures of a host of drugs or even to classify drugs. Instead, (1) it has pointed out how the phenomenal triumphs of chemotherapy have revolutionized the practice of medicine and extended life expectancy; (2) it has described how SAR and antimetabolite principles serve as guides in the search for new effective drugs; and (3) it has tried to show how the *lock-and-key* concepts of enzyme inhibition provides a fruitful picture of the mechanism of drug action. There is much more to be known about the mode of drug action and about biological processes. For instance, although aspirin is used more widely than any other therapeutic agent, its action in the body is little understood. Drugs are still sought and found by "test-and-see" methods. In spite of the vigorous search for antimalarials, malaria disables more people than any other disease. About a third of the world's population lives in malarial or previously malarial areas, and roughly 200 million are infected by malaria parasites with about 2 million lives being lost annually. Nevertheless, the fight continues with a spirit expressed by the words of Pasteur, "Science lives in successive solutions to problems of ever-increasing subtlety, approaching ever-nearer to the very essence of phenomena."

STUDY EXERCISES

1. What are three classes of microorganisms?
2. What is meant by the terms, chemotherapy, antibiotic, psychochemical, antimetabolite, SAR, and "lock and key" theory of drug action?
3. What is one special use of each of the following: (a) the sulfa drugs, (b) the antibiotics, (c) the psychochemicals, (d) vitamin or hormone feeding?
4. What are several physical and chemical properties of drugs that have been correlated with their biological activity?

Three-Hour Examination II

Again, a three-hour final examination is given, with answers, so that the student may test his proficiency. The larger sampling of material in the examination than is found with any set of Test Questions gives a better indication of the student's over-all "carryover" or "takeaway" training in the course.

I. How would you separate and isolate the five components in a mixture of *dextro-* and *levo-trans*-1,2-cyclohexane dicarboxylic acids, N-methylaniline, *p*-chloroaniline, and sucrose? Credit 15 pts.

II. Cite in a sentence or two a contribution to organic chemistry associated with the following names. If it is for a reaction, an equation for the reaction will serve best.

1. Wm. Perkin
2. H. C. Brown
3. R. W. Woodward
4. Cannizzaro
5. Sandmeyer
6. Kekulé
7. Emil Fischer
8. Beckmann
9. C. Hudson
10. L. Pauling

Credit 30 pts.

III. What are the monomers or raw materials used in the production of:

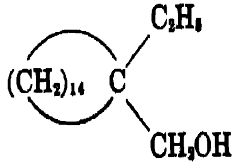
1. Orlon
2. Dacron
3. Teflon
4. Plexiglas
5. Nylon
6. Bakelite
7. Silicone oil?

Credit 10 pts.

IV. Explain the fact that acetone is essentially ketonic, ethyl acetoacetate is partially enolic, and phenol is not ketonic.

Or— Cite *factual evidence* to show that steric hindrance may affect the chemical and physical properties of molecules. Credit 20 pts.

V. Indicate the series of reactions you would use in the laboratory to prepare (a) *m*-fluorobenzoic acid starting with benzene and (b) compound I starting with any open-chain compound.



I

Credit 25 pts.

VI. What weight of crude iron would be used to reduce 1 mole of *m*-bromonitrobenzene to *m*-bromoaniline in dilute hydrochloric acid, if the iron is only 80% pure? Fe = 55.9. Credit 10 pts.

VII. In terms of resonance theory *or* molecular orbital theory, give the present concept of the structure of the benzene ring, and cite one piece of experimental evidence in support of this view. Credit 10 pts.

VIII. How would you distinguish by qualitative test-tube experiments:

1. Starch from cellulose
2. Benzylamine from toluidine
3. Cyclohexanol from phenol? Credit 10 pts.

IX. What are:

1. Three advantages and one disadvantage of synthetic textiles compared to natural textiles?
2. Three commercial products from cellulose?
3. Molecular sandwich compounds and inclusion compounds?
4. Three changes in public health brought about by the use of wonder drugs? Credit 20 pts.

X. In a reaction by which it was expected to obtain a trifluoromethyl ketone, CF_3COR, there were recovered two isomeric products A and B ($C_6H_5OF_3$). A and B each give a positive Baeyer unsaturation test, form 2,4-dinitrophenylhydrazones, and give a positive haloform test. A has strong infrared absorption bands at 1780, 1630 and 3510 cm^{-1}, and B has strong bands at 1730 and 1630 cm^{-1}. Assign structures to A and B and account for the infrared absorption bands. Credit 30 pts.

TOTAL SCORE 180 POINTS

ANSWERS TO THREE-HOUR EXAMINATION II

I. In this mixture, there are two acids, two bases, and a neutral compound. The neutral compound is water soluble and ether insoluble; hence, either water extraction or ether extraction of the mixture separates the sucrose. As a choice, let us ether extract the mixture, leaving behind the sucrose. Then, the ether solution is extracted with dilute hydrochloric acid to remove the bases. The aqueous phase is made alkaline, and the amines taken up in ether. The two amines are separated by the Hinsberg method: add benzenesulfonyl chloride to produce the respective benzenesulfonamides. The mixture of amides is extracted with alkali, which takes up the amide of the primary amine in the aqueous phase. The two separated amides may now be hydrolyzed separately in mineral acid, and the reaction mixtures made alkaline to liberate the free bases. They are insoluble and may be separated from the aqueous phases by mechanical means.

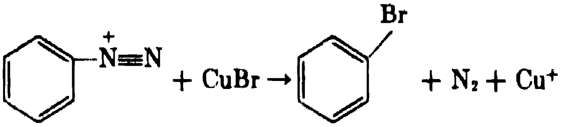
After the acid extraction to remove the bases, the initial ether solution will contain the optically active acids. These may be separated by adding an optically active base—strychnine, for example. Two diastereoisomeric salts would precipitate and could then be separated by fractional crystallization from a solvent such as acetone or alcohol. Addition of dilute hydrochloric acid to the separated salts will release the organic acids.

II. 1. Perkin: Initiated the commercial production of synthetic dyes.

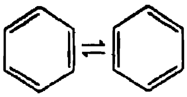
2. Brown was one of the first to obtain quantitative measurements of the magni-

tude of steric effects, and he proposed the concepts of F-strain and B-strain to account for the relative basicities of amines.

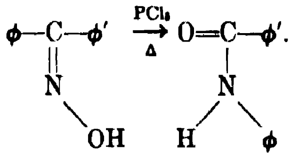
3. Woodward first developed the synthesis of several important natural products, including quinine, strychnine, and chlorophyll.
4. Cannizzaro: $2\phi\text{—CHO} + \text{conc. OH}^- \rightarrow \phi\text{—CO}_2^- + \phi\text{—CH}_2\text{OH}$.
5. Sandmeyer:



6. Kekulé, among many other things, proposed the first cyclic structure for benzene



7. Fischer, among many other things, showed that proteins are made up of many amino acids joined through peptide linkages. Won Nobel Prize in chemistry in 1902.
8. Beckmann:



$$\phi\text{—}\underset{\underset{\diagdown\text{OH}}{\text{N}}}{\overset{\|}{\text{C}}}\text{—}\phi' \xrightarrow[\Delta]{\text{PCl}_5} \text{O}{=}\underset{\underset{\text{H}\diagup\ \ \diagdown\phi}{\text{N}}}{\overset{|}{\text{C}}}\text{—}\phi'.$$

9. Hudson: Proposed rule by which one can determine the orientation of OH groups in sugars.
10. Pauling: Determined the helical structure of fibrous proteins by X-ray diffraction measurements; largely responsible for the concepts of orbital hybridization and resonance theory.

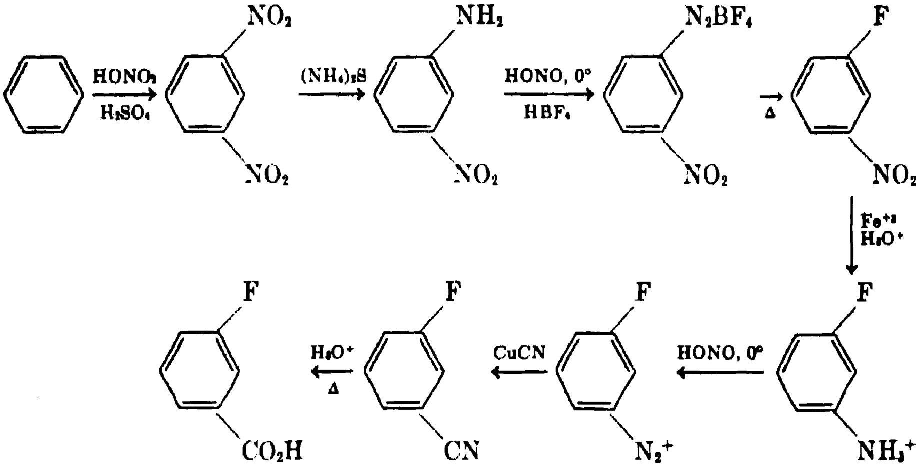
III. 1. Orlon: vinyl cyanide
  2. Dacron: dimethylphthalate + ethylene glycol
  3. Teflon: tetrafluoroethylene
  4. Plexiglas: esters of acrylic and methacrylic acids
  5. Nylon: hexamethylenediamine + adipic acid
  6. Bakelite: phenol + formaldehyde
  7. Silicone oil: alkyl halides + magnesium + silicon (or silicon tetrachloride)

IV. The summation of bond energies for acetone is greater than that of its tautomeric enol, and so much so that the enol form is not detected physically. In ethyl acetoacetate, an intramolecular hydrogen bond can occur which stabilizes the enol form sufficiently to be detected chemically. Phenol has the Kekulé resonance, which outweighs the greater summation of bond energies for the keto form to such an extent that the keto form is not detected by physical measurements.

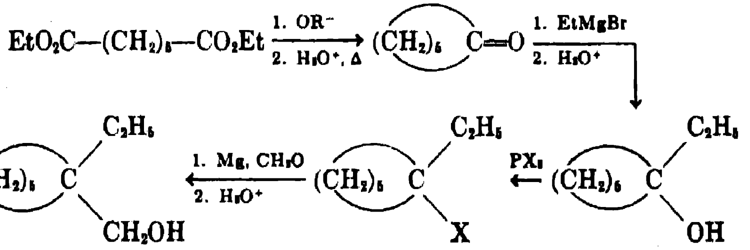
Or—Many examples can be given to show that steric hindrance affects the chemical properties of molecules. For instance, only aldehydes and methyl ketones add sodium bisulfite; benzoic and 2,6-dimethylphenylacetic acids may be esterified in alcoholic hydrochloric acid, but 2,6-dimethylbenzoic acid cannot; tetraphenylethylene adds

Cl_2 slowly, but does not add Br_2; and mesitylene will undergo a Friedel-Crafts reaction with methyl bromide, but not with *t*-butyl bromide. Two examples of steric hindrance affecting physical properties are (a) toward protonic and small acids, pyridine is a weaker base than trimethylamine, but toward a large acid like trimethylboron, pyridine is the stronger base, and (b) tetra-*ortho*-substituted biphenyls can be resolved into optically active isomers, but the corresponding *meta*- and *para*-substituted isomers cannot. (An explanation is not given here of why each of these examples demonstrates the effects of steric hindrance. A student's answer need include only one example of the effects of steric hindrance on chemical properties and one example on physical properties. Then he should explain why these effects can be attributed to steric hindrance.)

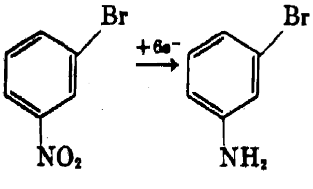
V. (a) Benzene to *m*-fluorobenzoic acid:



(b)



VI.



$$2Fe \xrightarrow{-6e^-} 2Fe^{+3}$$

Therefore, $\underset{1\ \text{mole}}{Br{-}C_6H_4NO_2} + \underset{2(55.9)\,g}{2Fe} \rightarrow Br{-}C_6H_4NH_2 + 2Fe^{+3}$

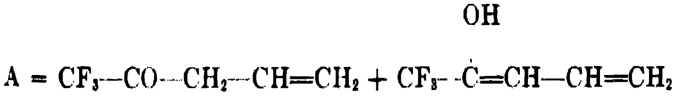
$$\frac{100}{80}(2 \times 55.9) = 140\ g$$

VII. The structure of the benzene ring is regarded as a composite of the two Kekulé structures. Support for this view comes from the facts that (a) the bond distances are all the same, intermediate between normal C—C and C═C distances, (b) the measured heats of formation are greater than that calculated for any single conceivable structural formula, and (c) Raman force constants of the carbon-carbon bonds of benzene are all identical, intermediate between normal C—C and C═C bond values. If the structure were either Kekulé structure alone, then some bond force constants and distances should be that of a regular C═C bond, and some of a regular C—C bond.

The molecular orbital picture is that of two inflated inner tubes, one on top of the other. They represent volumes in which there is an electron-cloud of π electrons or ring current over the carbon framework of the ring.

VIII. 1. Starch gives a blue coloration with iodine; cellulose does not.
2. Toluidine gives a deep-red color with alkali and benzenediazonium ion; benzylamine does not.
3. Phenol gives a purple color with aq. $FeCl_3$; cyclohexanol does not.

IX. 1. Advantages are tensile strength, dimensional stability, and resistance to mildew; one disadvantage is the static electricity frequently picked up by synthetic textiles.
2. Cellophane, collodion, and rayon.
3. Molecular sandwich compounds are complexes of organic compounds and metal ions in which the ion is located between two planar organic moieties, and the bonding between the ion and the organic portions is by intermolecular coordinate covalent bonding. Inclusion compounds are crystalline compounds in which one substance is trapped in the crystal cavities of a second substance.
4. Four types of wonder drugs are the sulfas, the antibiotics, the hormones, and the psychochemicals. The first two have reduced deaths from infections and deaths from diseases such as tuberculosis, pneumonia, diphtheria, and cholera to less than 10% of the 1935 rate. The hormones relieve patients of the painful symptoms of arthritis. The psychochemicals calm maniacs and other mentally ill patients, permitting them to be treated more effectively by psychiatrists. This has greatly reduced the number of mental patients in hospitals.

X. 

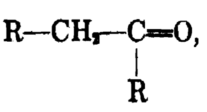
$A = CF_3—CO—CH_2—CH═CH_2 + CF_3—\overset{OH}{\overset{|}{C}}═CH—CH═CH_2$

$B = CF_3—CO—CH═CH—CH_3$

The infrared carbonyl frequencies are unusually high because of the large inductive effect of the CF_3 group.

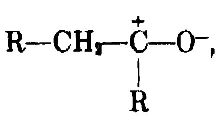
Summarizing Statement

It can be seen that the chemical, physical, and to a limited extent the biochemical properties of molecules are understood in terms of structural formulas. These formulas are gross representations of the electric charge distributions of the molecules, for atoms are nothing but assemblages of positively charged nuclei and the surrounding negatively charged electrons. In many cases, a single structural formula cannot be given for a compound which is consistent with all the observed properties, and a theory called resonance is employed. This is a concept in which the molecule is regarded as a composite of several structural formulas, the actual structure having a certain resemblance to each of the proposed structures. For illustration, to account for the physical properties of ketones, such as dipole moments, carbon-oxygen bond distances, and polar character, and to account for the chemical properties, such as 1,2-addition to the C═O bond and reactions involving the α-carbon atom, ketones are regarded as resonance hybrids of structures I, II, and III.



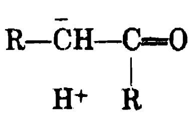
$\mathrm{R{-}CH_2{-}\underset{\displaystyle R}{\underset{|}{C}}{=}O}$,

I



$\mathrm{R{-}CH_2{-}\underset{\displaystyle R}{\underset{|}{\overset{+}{C}}}{-}O^-}$,

II

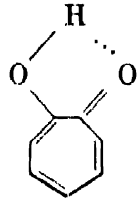


$\mathrm{R{-}\underset{\displaystyle H^+}{\underset{|}{\overset{-}{CH}}}{-}\underset{\displaystyle R}{\underset{|}{C}}{=}O}$

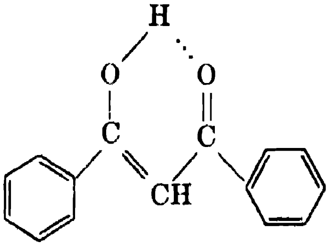
III

At the same time, it is realized that certain other structural features of molecules must be considered when using structural formulas, even when the concept of resonance is adopted. Thus, inductive effects, hydrogen bonding, and steric requirements are significant factors to be recognized. For illustration, the large acid strength of trichloroacetic acid is due to the inductive effect of the chlorine atoms, and, without recognition of this factor, one would expect CCl_3COOH and CH_3COOH to have about the same acid strengths. Due to the powerful inductive effect of fluorine, for instance, perfluoro ethers are such weak bases that they cannot be hydrolyzed in hydriotic acid and will not form stable salts with the strong acid BF_3; perfluoro amides do not undergo the Hofmann degradation to amines; perfluoro secondary alcohols, $(C_nF_{2n+1})_2CHOH$, are as acidic as phenols; and CF_3I reacts with KOH to yield $CF_3H + KOI$ instead of the expected $CF_3OH + KI$. These physical and chemical properties are not predictable from the structural formulas without incorporating the inductive effect.

Similarly, it has been shown that steric requirements markedly affect physical and chemical properties of molecules. For instance, the base strength of certain amines toward various acids, the rate and ease of reaction of so-called hindered acids and esters, the barrier to 1,2-addition to $C{=}C$ and $C{=}O$ groups in alkenes and ketones with large substituents, and the optical isomerism of *ortho*-substituted biphenyls have all been explained in the text in terms of steric relationships. Also, the effects of hydrogen bonding on physical and chemical properties were pointed out on different occasions. For instance, the effects on boiling points, solubilities, steam distillability, enol-keto equilibria, and adsorption of hydroxylic and amino compounds were discussed. Hydrogen bonds may also affect chemical properties. For example, tropolone and dibenzoylmethanes have strong intramolecular hydrogen bonds which "tie up" the OH and $C{=}O$ groups so tightly that the OH is not acetylated with acetic anhydride and the $C{=}O$ group does not form a Schiff base with even 2,4-dinitrophenylhydrazine.



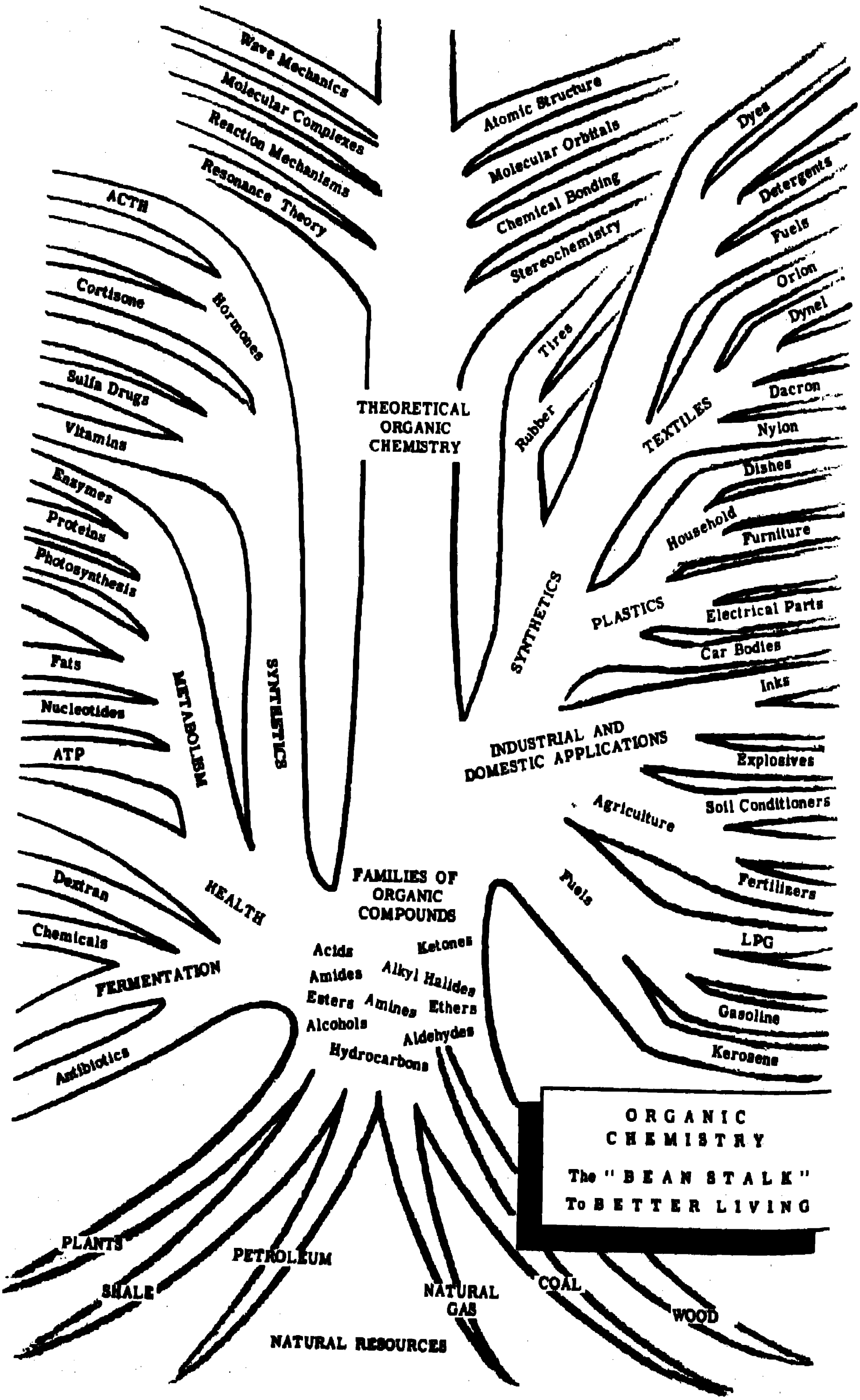
Tropolone



Enol structure of dibenzoylmethane

So it is, the properties of molecules are interpreted and predicted in terms of structural formulas plus the concepts of resonance, induction, hydrogen bonding, steric relations, solvation, and molecular orbitals. This multi-effect approach has been called the "Modern Structural Theory of Organic Chemistry." In studying organic chemistry, the student first learns the chemical and physical properties associated with the more common functional groups or classes of compounds. Slowly he learns to incorporate the effects of resonance, induction, etc., and gradually is able to understand the behavior of organic molecules and even predict certain not yet measured properties. This familiarity with the behavior of organic molecules in terms of the modern structural theory of organic chemistry should be developed irrespective of the student's future work, i.e., medicine, dentistry, agriculture, pharmacy, or professional chemistry.

One might ask, Why must a premedical student learn so many organic reactions? This can be answered in the following way. It is not expected that


ORGANIC CHEMISTRY
The "BEAN STALK" To BETTER LIVING
THEORETICAL ORGANIC CHEMISTRY
Wave Mechanics
Molecular Complexes
Reaction Mechanisms
Resonance Theory
Atomic Structure
Molecular Orbitals
Chemical Bonding
Stereochemistry
ACTH
Cortisone
Hormones
Sulfa Drugs
Vitamins
Enzymes
Proteins
Photosynthesis
Fats
Nucleotides
ATP
METABOLISM
SYNTHETICS
HEALTH
Dextran
Chemicals
FERMENTATION
Antibiotics
Tires
Rubber
SYNTHETICS
Dyes
Detergents
Fuels
Orlon
Dynel
TEXTILES
Dacron
Nylon
Dishes
Household
Furniture
PLASTICS
Electrical Parts
Car Bodies
Inks
INDUSTRIAL AND DOMESTIC APPLICATIONS
Explosives
Soil Conditioners
Agriculture
Fertilizers
Fuels
LPG
Gasoline
Kerosene
FAMILIES OF ORGANIC COMPOUNDS
Acids
Ketones
Amides
Alkyl Halides
Esters
Amines
Ethers
Alcohols
Aldehydes
Hydrocarbons
PLANTS
SHALE
PETROLEUM
NATURAL GAS
COAL
WOOD
NATURAL RESOURCES

the student will long remember all of the reactions taken up in the one year. However, he takes up a fairly wide variety of reactions to give him a strong impression of the general behavior of organic substances, and solves a large number of organic problems of varying complexity to appreciate and acquire some skill in attacking problems in which certain data are at hand (symptoms in a medical problem) and one must use deductions and judgments in reaching a solution. After all, most of the reactions which take place in all living systems are organic. In recent years, medicine and nature are being investigated and explained more and more in terms of fundamental chemistry and physics. Some of the most outstanding recent triumphs over mental disorders have been through organic chemistry. Just as the organic chemist refers to reactions by name, i.e., Friedel-Crafts', Sandmeyer, etc., so does a physician refer to diseases, tests and treatments by name. A chemist need not specify all the reagents he uses in a certain reaction, he merely names the reaction and a given starting compound. Similarly, a physician does not cite all of the symptoms of a patient to another doctor, he merely gives the name of the disease. The experience and associations in elementary organic chemistry train the student to develop thought patterns useful for advanced organic chemistry as well as for medical or other careers. Of course, considerable supplementary material is also taken up, such as the uses, nomenclature, and commercial applications of organic chemicals. Some of this is necessary to provide an appreciation for the economic importance of organic chemicals and the important role which these chemicals play in our daily lives. This last aspect was emphasized in the introduction to this book.

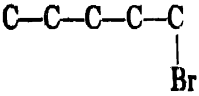
As a final statement, it is hoped that the student's picture of organic chemistry is clearer than that of Friedrich Wöhler when he wrote, more than a century ago, "Organic chemistry nowadays almost drives me mad. To me it appears like a primeval tropical forest, full of the most remarkable things; a dreadful, endless jungle into which one does not dare enter, for there seems to be no way out."

Answers to Test Questions

Set 1 (page 52)

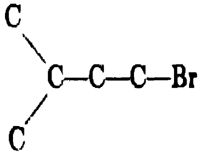
1. Best answer: Isohexane. Other possible answers: 2-methylpentane; dimethyl-*n*-propylmethane; ethyl-isopropylmethane; isobutylmethylmethane.

2. Three carbon skeletons possible; just place the bromine atom on different carbon atoms:

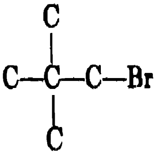


$\mathrm{C{-}C{-}C{-}C{-}\underset{\displaystyle Br}{\underset{|}{C}}}$

1-Bromopentane
(3 isomers)



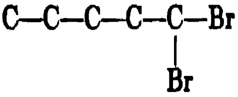
1-Bromo-3-methylbutane
(4 isomers)



$\mathrm{C{-}\overset{\displaystyle C}{\underset{\displaystyle C}{C}}{-}C{-}Br}$

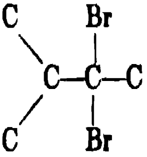
1-Bromo-2,2-dimethylpropane

3. Three carbon frameworks possible; suggested answers are

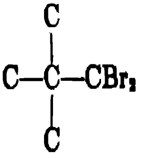


$\mathrm{C{-}C{-}C{-}C{-}\underset{\displaystyle Br}{\underset{|}{C}}{-}Br}$

(1,1-Dibromopentane)



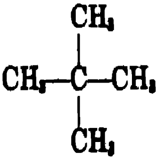
2,2-Dibromo-3-methylbutane
(10 isomers with this carbon skeleton)



$\mathrm{C{-}\overset{\displaystyle C}{\underset{\displaystyle C}{C}}{-}CBr_2}$

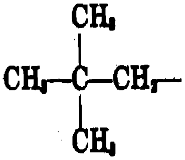
1,1-Dibromo-2,2-dimethylpropane
(2 isomers with this carbon skeleton)

4.



$\mathrm{CH_3{-}\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}{-}CH_3}$

Neopentane



$\mathrm{CH_3{-}\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}{-}CH_2{-}}$

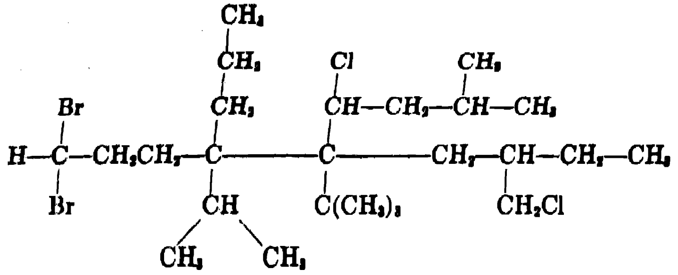
Neopentyl group

5. a, c, and g; b, e, and h.

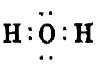
6. (a) $\mathrm{CH_3{-}C(CH_3)_2{-}CH(CH_3){-}CH_2CH_2CH_3}$
   (b) $\mathrm{CH_3CH_2{-}CH(CH_3){-}CH(CH_2CH_2CH_3){-}CH_2CH_2CH_2CH_3}$
   (c) $\mathrm{(CH_3)_2CH{-}CH_2CH_2CH_3}$
   (d) $\mathrm{(CH_3)_3C{-}CH_2CH_3}$

7. 2,7-Dimethyl-3,3-dichloro-4-sec-butyl-4-isopropyl-5-*n*-butyl-5-isobutyl-6-bromo-6-chloromethylnonane.

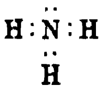
8.



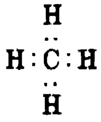
9.



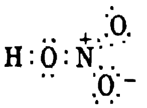
H_2O



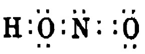
NH_3



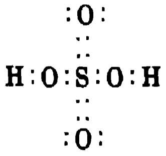
CH_4



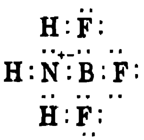
$HONO_2$



HONO



H_2SO_4



$H_3N—BF_3$

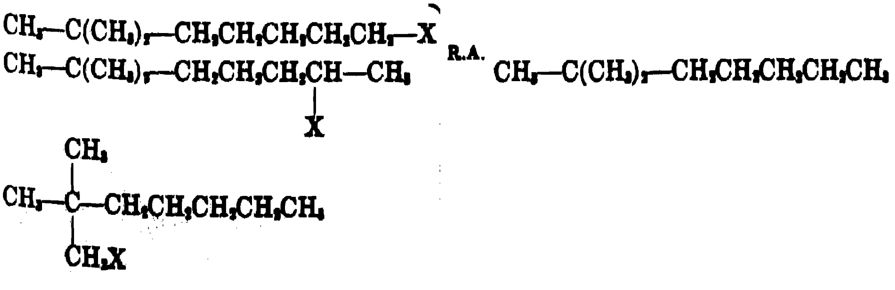
10. Since $C_e/C_w = 10$, then if brine is used, the compound will not be as soluble in brine as in water and the coefficient will be larger.

Set 2 (page 87)

1. The gas could be passed through chambers or tubes containing a substance to absorb the impurities but not react with methane. Thus, bases such as the metal hydroxides would remove the HCl, and drying agents such as anhydrous KOH, K_2CO_3, $CaCl_2$, etc., would take up the water vapor.

2. No, because homologs do not have the same molecular formulas.

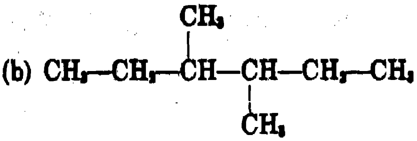
3. (a) 2,2-Dimethylheptane could be produced by reducing a suitable alkyl halide. In this case the starting compound could be one in which any of the hydrogen atoms of the product has replaced a halogen atom, e.g.,



$$CH_3-C(CH_3)_2-CH_2CH_2CH_2CH_2CH_2-X$$

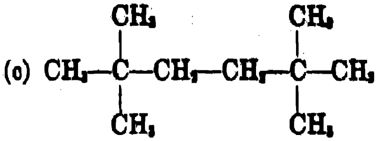
$$CH_3-C(CH_3)_2-CH_2CH_2CH_2\underset{X}{CH}-CH_3 \xrightarrow{R.A.} CH_3-C(CH_3)_2-CH_2CH_2CH_2CH_2CH_3$$

$$CH_3-\overset{CH_3}{\underset{CH_2X}{C}}-CH_2CH_2CH_2CH_2CH_3$$



(b) $CH_3-CH_2-\overset{CH_3}{CH}-\underset{CH_3}{CH}-CH_2-CH_3$

3,4-Dimethylhexane

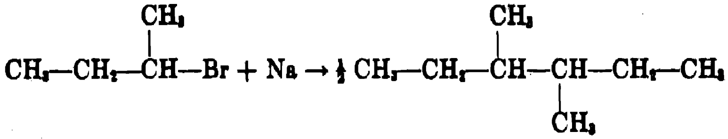


(c) $CH_3-\overset{CH_3}{\underset{CH_3}{C}}-CH_2-CH_2-\overset{CH_3}{\underset{CH_3}{C}}-CH_3$

2,2,5,5-Tetramethylhexane

Since these are symmetrical alkanes, representable by the formula R—R, each one may be synthesized using any of the three general reactions given in this chapter. One half of the product molecule is designated R.

E.g.:

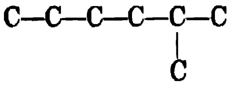


$CH_3-CH_2-\overset{CH_3}{CH}-Br + Na \rightarrow \tfrac{1}{2}\, CH_3-CH_2-\overset{CH_3}{CH}-\underset{CH_3}{CH}-CH_2-CH_3$

$CH_3-C(CH_3)_2-CH_2-CO_2Na \xrightarrow{\text{electrolysis}} CH_3-C(CH_3)_2-CH_2CH_2-C(CH_3)_2-CH_3$

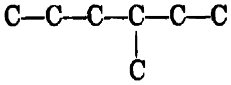
4. $CH_3CH_2CH_2CH_2CH_2CO_2Na \xrightarrow{\text{electrolysis}} CH_3-(CH_2)_8-CH_3$

5. Start with straight chain carbon skeleton, *n*-heptane. Then work with six-carbon chain moving a methyl group around, e.g.,



$C-C-C-C-\underset{C}{C}-C$

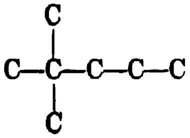
2-Methylhexane



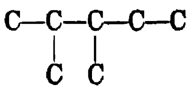
$C-C-C-\underset{C}{C}-C-C$

3-Methylhexane

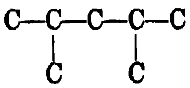
Now, take five-carbon chain and move two methyl groups around:



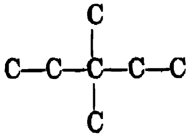
$C-\overset{C}{\underset{C}{C}}-C-C-C$



$C-\underset{C}{C}-\underset{C}{C}-C-C$

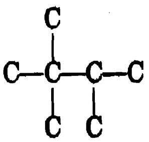


$C-\underset{C}{C}-C-\underset{C}{C}-C$



$C-C-\overset{C}{\underset{C}{C}}-C-C$

and four-carbon chain to move three methyl groups around:



$C-\overset{C}{\underset{C}{C}}-\underset{C}{C}-C$

The names are easily given by the I.U.C. system.

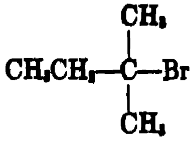
6. $CH_3CH_3 \xrightarrow[\Delta]{Cl_2} CH_3CH_2-Cl \xrightarrow{Na} CH_3CH_2CH_2CH_3$

7. C_5H_{12}; $C_{10}H_{22}$; C_3H_7 to C_3H_8; C_2H_4 to C_2H_6; C_4H_9 to C_4H_{10}; $C_{11}H_{23}$ to $C_{11}H_{24}$
8. 4.5 liters excess O_2; 16.4 g H_2O.
9. 2.1 liters.
10. 2.22 *N*.
11. C_6H_{14}. (a) 2,3-Dimethylbutane; (b) *n*-hexane and neohexane; (c) 3-methyl-

pentane. (a) will give six dibromo derivatives; (b) *n*-hexane, 12, and neohexane, 7; (c) 12.

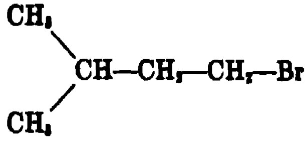
12. (a) 0.703, (b) 0.730, (c) 0.749.

13.



$CH_3CH_2-C(CH_3)_2-Br$

A



$(CH_3)_2CH-CH_2-CH_2-Br$

B

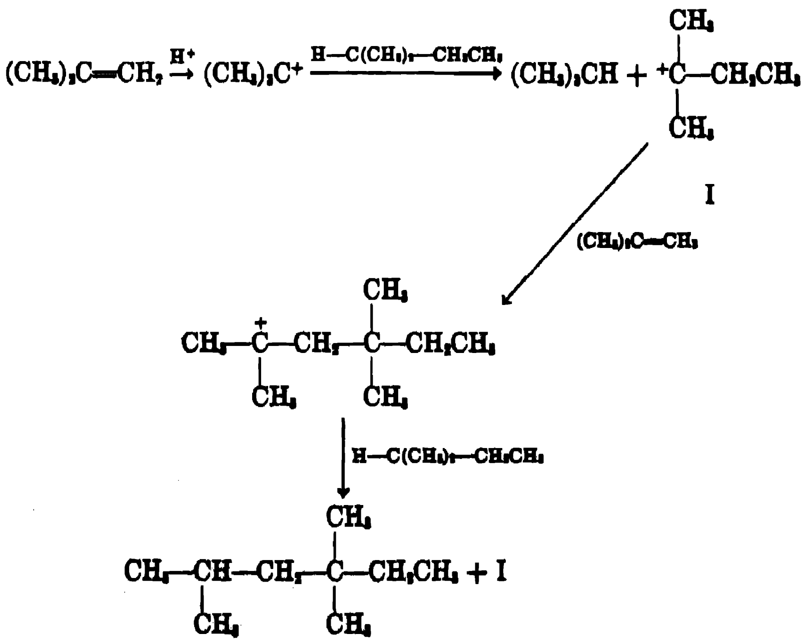
14. If isobutyl bromide were used in a Wurtz reaction, it would produce 2,5-dimethylhexane. sec-Butyl bromide would yield 3,4-dimethylhexane. Comparison of the propertues of either product with that of the unknown would identify the unknown. One could compare their indexes of refraction, infrared absorption spectra, or some other physical property.

15. Halogenation proceeds by a halogen atom abstracting a hydrogen atom from the organic molecule. The more electronegative is the group Z in $Z-CH_3$, the more it pulls electrons from the carbon atom, which, in turn, more strongly holds its electrons shared with the hydrogen atoms. This makes it more difficult for a halogen atom to pull a hydrogen atom from the carbon to bring about halogenation.

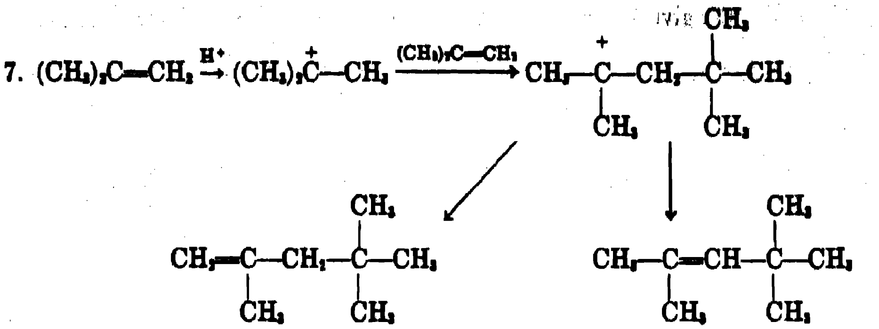
Set 3 (page 126)

1. $CH_3CH_2-CHCl-CH_2-CH(CH_3)_2$
2. 2-Chlorohexane, $CH_3-CHCl-CH_2CH_2CH_2CH_3$
3. 41% yield; 26.8 g Zn.
4. $(CH_3CH_2)_2C=CH-CH(CH_3)_2$
5. With vapor pressure of H_2O = 23.8 mm at 25°, 28.1 liters ethylene; 28.1 kl.

6.



$(CH_3)_2C=CH_2 \xrightarrow{H^+} (CH_3)_3C^+ \xrightarrow{H-C(CH_3)_2-CH_2CH_3} (CH_3)_3CH + {}^+C(CH_3)_2-CH_2CH_3$
I
$(CH_3)_2C=CH_2$
$CH_3-\overset{+}{C}(CH_3)-CH_2-C(CH_3)_2-CH_2CH_3$
$H-C(CH_3)_2-CH_2CH_3$
$CH_3-CH(CH_3)-CH_2-C(CH_3)_2-CH_2CH_3 + I$

7. 

$$(CH_3)_2C{=}CH_2 \xrightarrow{H^+} (CH_3)_2\overset{+}{C}{-}CH_3 \xrightarrow{(CH_3)_2C{=}CH_2} CH_3{-}\overset{+}{C}(CH_3){-}CH_2{-}C(CH_3)_2{-}CH_3$$

$$CH_2{=}C(CH_3){-}CH_2{-}C(CH_3)_2{-}CH_3 \qquad CH_3{-}C(CH_3){=}CH{-}C(CH_3)_2{-}CH_3$$

2,4,4-Trimethyl-1-pentene
Minor product

2,4,4-Trimethyl-2-pentene
Major product

8. 22.4 liters.

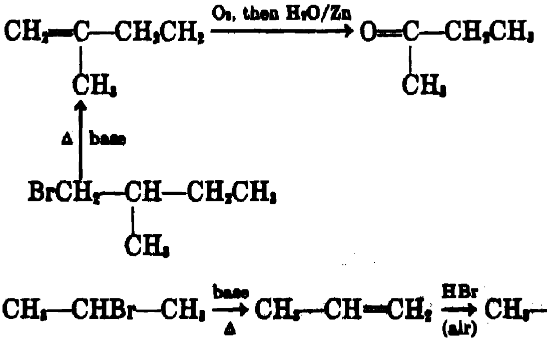
9. By treating the sample with Br_2/CCl_4 dropwise and noting the rapid decolorization of the bromine solution, by treating the sample with dil. aq. $KMnO_4$ dropwise and noting the rapid removal of color of the permanganate solution, or by suspending a few drops of the sample in conc. H_2SO_4 and observing whether or not the drops dissolve. The alkene gives a positive reaction in all three cases, whereas the alkane would be inert.

10. 25 ml.

11. (a) $CH_3CH_2CH_2Br \xrightarrow[\Delta]{base} CH_3CH{=}CH_2 \xrightarrow{Cl_2} CH_3{-}CHCl{=}CH_2Cl$

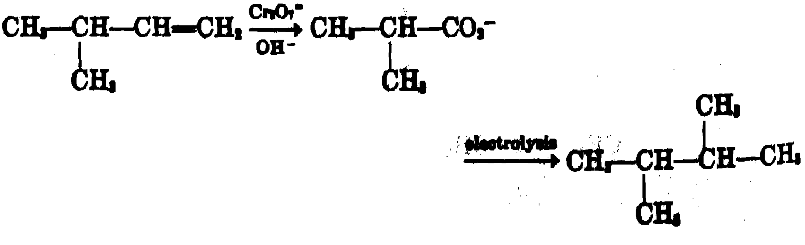
(b) $CH_3{-}CHOH{-}CH_3 \xrightarrow{H_2SO_4} CH_3{-}CH{=}CH_2 \xrightarrow[(air)]{HBr} CH_3{-}CH_2{-}CH_2Br$

(c) $CH_3CH_2Br \xrightarrow[\Delta]{base} CH_2{=}CH_2 \xrightarrow{HOCl} CH_2Cl{-}CH_2OH$

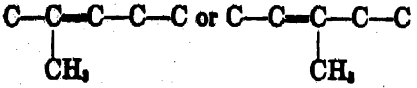
(d) 

$$BrCH_2{-}CH(CH_3){-}CH_2CH_3 \xrightarrow[\Delta]{base} CH_2{=}C(CH_3){-}CH_2CH_3 \xrightarrow{O_3,\ then\ H_2O/Zn} O{=}C(CH_3){-}CH_2CH_3$$

(e) $CH_3{-}CHBr{-}CH_3 \xrightarrow[\Delta]{base} CH_3{-}CH{=}CH_2 \xrightarrow[(air)]{HBr} CH_3{-}CH_2{-}CH_2{-}Br \xrightarrow[\Delta]{Na}$ *n*-Hexane

(f) 

$$CH_3{-}CH(CH_3){-}CH{=}CH_2 \xrightarrow[OH^-]{Cr_2O_7^{=}} CH_3{-}CH(CH_3){-}CO_2^- \xrightarrow{electrolysis} CH_3{-}CH(CH_3){-}CH(CH_3){-}CH_3$$

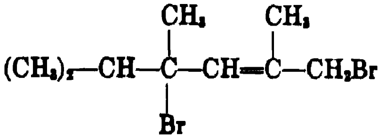
12. 

$C-\underset{CH_3}{C}=C-C-C$ or $C-C=\underset{CH_3}{C}-C-C$

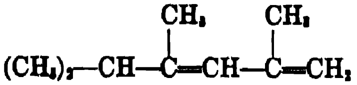
If treated with ozone, then H_2O, the former alkene will give $CH_3-\underset{CH_3}{C}=O$ + $O=CH-CH_2CH_3$, whereas the latter alkene would give $CH_3-CH=O$ plus $O=\underset{CH_3}{C}-CH_2CH_3$. By determining which set of carbonyl products is produced (through derivatives as will be shown later) one can deduce the structure of the original alkene.

13. R = $CH_3-CBr_2-CH_2-CH(CH_3)_2$ or $CH_3-CHBr-CHBr-CH(CH_3)_2$
S = $CH_3-C\equiv C-CH(CH_3)_2$

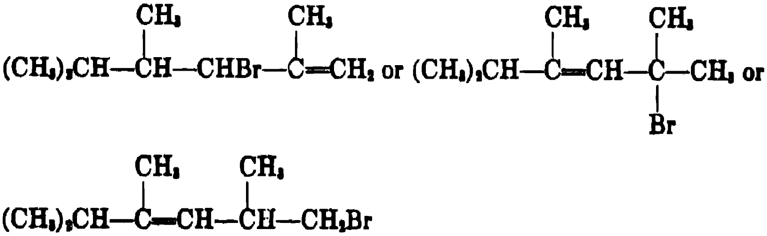
14. 583 g.

15. Y = 

$(CH_3)_2-CH-\underset{Br}{\overset{CH_3}{C}}-CH=\overset{CH_3}{C}-CH_2Br$

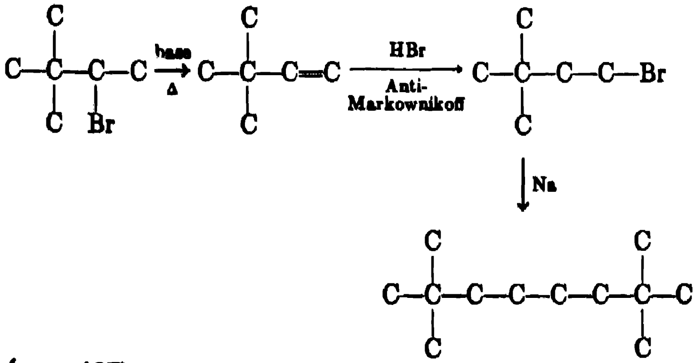
X = 

$(CH_3)_2-CH-\overset{CH_3}{C}=CH-\overset{CH_3}{C}=CH_2$

W = 

$(CH_3)_2CH-\overset{CH_3}{C}H-CHBr-\overset{CH_3}{C}=CH_2$ or $(CH_3)_2CH-\overset{CH_3}{C}=CH-\underset{Br}{\overset{CH_3}{C}}-CH_3$ or

$(CH_3)_2CH-\overset{CH_3}{C}=CH-\overset{CH_3}{C}H-CH_2Br$

16. 

$$C-\underset{C}{\overset{C}{C}}-\underset{Br}{C}-C \xrightarrow[\Delta]{base} C-\underset{C}{\overset{C}{C}}-C=C \xrightarrow[\text{Anti-Markownikoff}]{HBr} C-\underset{C}{\overset{C}{C}}-C-C-Br$$

$$\xrightarrow{Na} C-\underset{C}{\overset{C}{C}}-C-C-C-C-\underset{C}{\overset{C}{C}}-C$$

Set 4 (page 137)

1. Propene, methylacetylene, water, acetic acid.
2. 12.6 liters.
3. (a) Pass the gases through an aqueous alkaline solution of $KMnO_4$, which will oxidize the unsaturated hydrocarbons to water-soluble products, then pass the gas through a tube containing a drying agent such as $CaCl_2$, Na_2SO_4, K_2CO_3, BaO, P_2O_5, or even H_2SO_4.

(b) Pass the gases through an ammoniacal cuprous chloride solution to precipitate the propyne.

4. Treat a sample with ammoniacal cuprous chloride; if a precipitate is formed, the compound is 1-hexyne. In case of a negative reaction, test for unsaturation with Br_2/CCl_4 or with aq. $KMnO_4$. A positive reaction indicates 1-hexene, and a negative reaction, *n*-hexane.

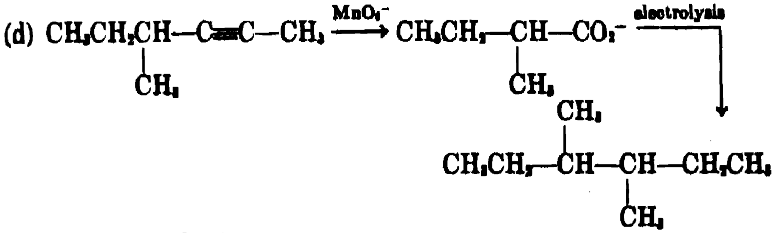
5. 16.3 g.

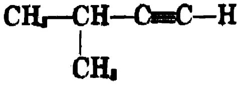
6. Treat the sample with maleic anhydride in ether. The 1,3-butadiene should undergo the Diels-Alder reaction and form a precipitate.

7. (a) $CH_3—CHOH—CH_3 \xrightarrow{H_2SO_4} CH_3—CH{=}CH_2 \xrightarrow{Br_2} CH_3—CHBr—CH_2Br \xrightarrow{KOH_{alc.}} CH_3—C{\equiv}CH$

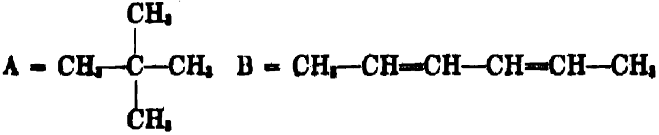
(b) $CH_3—CH_2—CH{=}CH_2 \xrightarrow{Br_2} CH_3CH_2CHBr—CH_2Br \xrightarrow[2.\ HCl\ aq.]{1.\ NaNH_2\ excess} CH_3CH_2C{\equiv}CH$

(c) $CH_3CH_2CH_2CH_2CH_2Br \xrightarrow[\Delta]{base} CH_3CH_2CH_2CH{=}CH_2 \xrightarrow{Br_2} CH_3CH_2—CH_2CHBr—CH_2Br \xrightarrow[2.\ HCl\ aq.]{1.\ NaNH_2\ excess} CH_3CH_2CH_2—C{\equiv}CH$

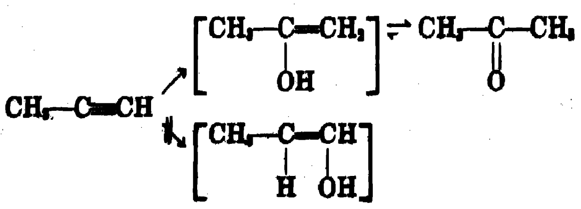

(d) $CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{CH}}—C{\equiv}C—CH_3 \xrightarrow{MnO_4^-} CH_3CH_2—\underset{\displaystyle CH_3}{\underset{|}{CH}}—CO_2^- \xrightarrow{electrolysis} CH_3CH_2—\overset{\displaystyle CH_3}{\overset{|}{CH}}—\underset{\displaystyle CH_3}{\underset{|}{CH}}—CH_2CH_3$

8.

$CH_3—\underset{\displaystyle CH_3}{\underset{|}{CH}}—C{\equiv}C—H$

9. Linear.

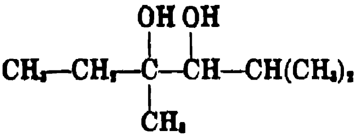
10.

$A = CH_3—\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle CH_3}{\overset{|}{C}}}}—CH_3 \quad B = CH_3—CH{=}CH—CH{=}CH—CH_3$

$C = CH_3—C{\equiv}C—CH_2CH_2CH_3$ or $CH_3CH_2—C{\equiv}C—CH_2CH_3$

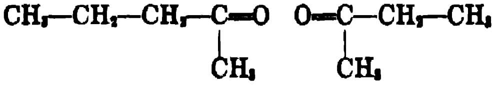
11.

$$CH_3—C{\equiv}CH \nearrow \left[CH_3—\underset{\displaystyle OH}{\underset{|}{C}}{=}CH_2\right] \rightleftharpoons CH_3—\underset{\displaystyle O}{\underset{\|}{C}}—CH_3$$
$$CH_3—C{\equiv}CH \searrow \left[CH_3—\underset{\displaystyle H}{\underset{|}{C}}{=}\underset{\displaystyle OH}{\underset{|}{CH}}\right]$$

Set 5 (page 161)

1. $HO_2C-(CH_2)_4-COOH$. Used as one of the monomers for making nylon.
2. No.
3. *trans*-1,3-Dibromocyclohexane.
4. 2-Pentene would rapidly decolorize cold, alkaline permanganate solution and cold Br_2/CCl_4 solution. 1,2-Dimethylcyclopropane would decolorize the bromine solution but not the permanganate. Cyclopentane would not react with either reagent at a reasonable rate under these conditions.
5. The explanation is somewhat similar to the discussion on page 154 describing the addition of bromine to this pair of acids, except that the hydroxylation is *cis* rather than *trans* and an inversion does not occur.

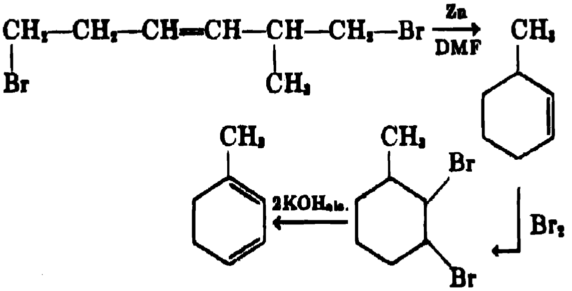
6. 

$CH_3-CH_2-C(OH)(CH_3)-CH(OH)-CH(CH_3)_2$

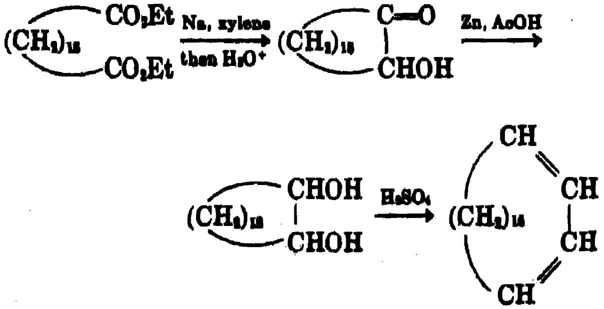
7. 

$CH_3-CH_2-CH_2-C(CH_3){=}O \quad O{=}C(CH_3)-CH_2-CH_3$

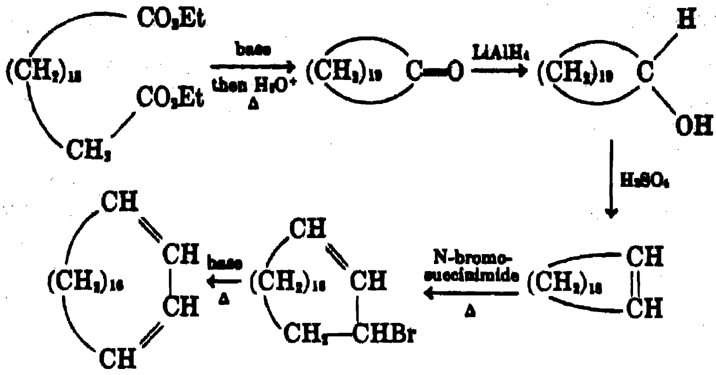
8. A = neopentane, B = cyclohexene, C = 1-hexyne

9. 

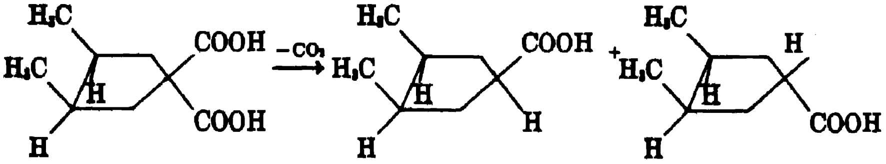
10. 49.8% yne, 24.9% ene, and 25.3% ane.

11. 

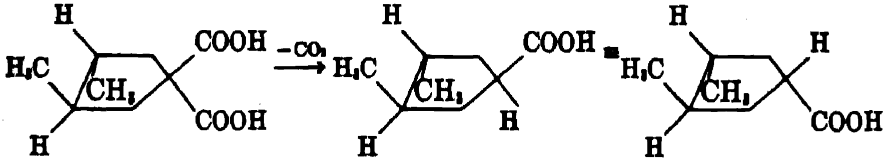
An alternative but longer route is:



12.



A



B

13. The *cis* isomer, because the leaving groups, H and tosylate, are diaxial.

Set 6 (page 176)

1. It must be symmetrical; O═C═O.

2. CH_4 and CCl_4 are symmetrical and the bond moments cancel one another. CH_3Cl is unsymmetrical, and therefore it has a resultant moment.

3. Yes.

4. Compounds I and II have the same chromophoric system, since the $C_6H_5CH{=}CH—$ groups in II are not conjugated. The groups are conjugated in III, and therefore III will have a much larger λ_m.

5. Ratio = 1:1:3:3, all singlets, since carbons alpha to each proton contain no H's.

6. 2.82τ, phenyl group, singlet; 5.56τ, methine, quartet; 8.57τ, methyl, doublet.

7. The C═S bond is a strong chromophore and makes compounds blue. $(C_2H_5)_2C{=}S$ tautomerises to $CH_3{-}CH{=}\underset{SH}{\underset{|}{C}}{-}CH_2CH_3$, which is more stable than the thioketone because of the weakness of the C═S bond. The thioenol now lacks a strong chromophore. Sulfur and the second-row elements do not readily form multiple bonds. This gives the C═S bond a large $^+C—S^-$ character from the resonance, C═S, $^+C—S^-$. The thioketone therefore has a substantial dipole moment, larger than that of the corresponding ketones.

8. The singlet in the spectrum of ethyl acetate is the middle band, whereas it

appears the farthest downfield (lowest τ value) in the spectrum of methyl propionate.

Set 7 (page 207)

1. $C_6H_6 \xrightarrow{HNO_3-H_2SO_4} C_6H_5NO_2 \xrightarrow[150^\circ]{Cl_2,\ Fe} m\text{-}ClC_6H_4NO_2$

$C_6H_6 \xrightarrow[60^\circ]{Br_2,\ Fe} C_6H_5Br \xrightarrow{HNO_3,\ H_2SO_4} (o + p)\text{-}BrC_6H_4NO_2$

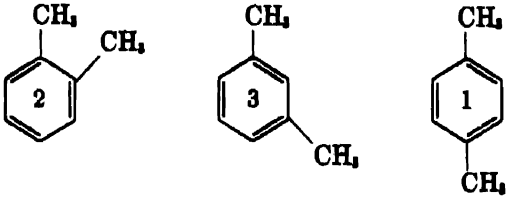
$C_6H_6 \xrightarrow{CH_3Br,\ AlCl_3} C_6H_5CH_3 \xrightarrow{HNO_3,\ H_2SO_4} (o + p)\text{-}H_3CC_6H_4NO_2$

2. By treating a sample with cold $KMnO_4$ aq. or Br_2/CCl_4 solution. In either case, the cyclohexene would react rapidly, evidenced by a disappearance of the color of the reagent, whereas the benzene would be unaffected.

3. 20%.

4. Et—CO—CO—H: Me—CO—CO—H: H—CO—CO—H = 1:1:1

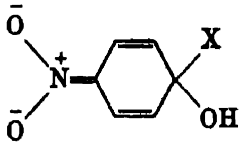
5.



Each gives a different number of mono-substitution products. This fact is the basis of this direct method of distinguishing the isomers often used by early organic chemists.

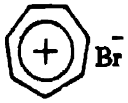
6. 1541 kcal/mole.

7. When the OH⁻ ion attacks the nitrohalobenzene, the *ortho* or *para* nitro group can accommodate the negative charge as in the insipient structure



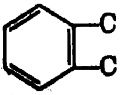
This stabilisation of the reaction transition state lowers the activation energy which facilitates reaction.

8. Its solubility properties and immediate reaction with Ag^+ indicates it is ionic. Hence, the $C_7H_7^+$ ion is stable, presumably the tropylium ion. The isomeric benzyl carbonium ion is not as stable.

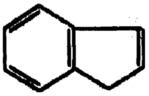


C_7H_7Br

9. C_9H_8 unsaturated with one olefinic bond. R gives C_9H_{16}, which must have two rings. R yields phthalic acid; hence it must have in its structure



Adding the double bond and the second ring to fit C_9H_8, we get:



10. Pyridine: bond strain makes *c* very unstable. Pyrrole and fluorobenzene: N and F cannot accommodate 10 electrons in their valence shells as indicated by *c*. A ketone: oxygen is more electronegative than carbon and withdraws the π electrons.

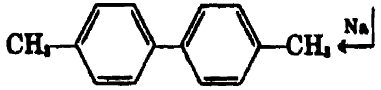
Set 8 (page 220)

1. (a) $C_6H_6 \xrightarrow{CH_3Br,\ AlCl_3} C_6H_5CH_3 \xrightarrow[\Delta]{Br_2,\ h\nu} C_6H_5CH_2Br$

(b) $C_6H_6 \xrightarrow{EtX,\ AlCl_3} C_6H_5\,Et \xrightarrow{Cl_2,\ Fe} (o + p)\text{-}ClC_6H_4Et$

(c) $C_6H_6 \xrightarrow{CH_3X,\ AlCl_3} C_6H_5CH_3 \xrightarrow{Br_2,\ Fe} (o + p)\text{-}BrC_6H_4CH_3$

Take *p*-isomer



(d) $C_6H_6 \xrightarrow{2(CH_3)_2CHBr,\ AlCl_3} p\text{-}(CH_3)_2CHC_6H_4CH(CH_3)_2 \xrightarrow[\text{then } H^+]{6KMnO_4,\ OH^-} p\text{-}(CH_3)_2CHC_6H_4CO_2H$

(e) $C_6H_6 \xrightarrow[AlCl_3]{CH_3Br} C_6H_5CH_3 \xrightarrow[\text{then } H^+]{KMnO_4 \text{ excess},\ OH^-} C_6H_5CO_2H \xrightarrow[H_2SO_4]{HNO_3} m\text{-}O_2N{-}C_6H_4CO_2H$

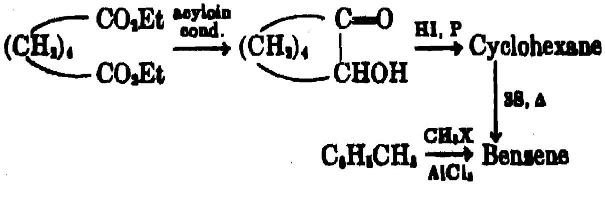
(f) $C_6H_6 \xrightarrow{CH_3Br{-}AlCl_3} C_6H_5CH_3 \xrightarrow{HNO_3{-}H_2SO_4} (o + p)\text{-}O_2NC_6H_4CH_3$

(take *p*-isomer)

$p\text{-}O_2NC_6H_4CO_2H \xleftarrow[\text{then } H^+]{KMnO_4,\ OH^-}$

2. Each phenyl ring of biphenyl has a resonance energy essentially equal to that of benzene and, hence, the total resonance energy of biphenyl is greater than that of benzene by an amount corresponding to the degree of resonance interaction between rings. This is small for the ground state of biphenyl.

3. Heat the sample with sulfur; hexane undergoes dehydrogenation to liberate H_2S, which has an odor easily recognized. Or heat the sample with a little alkaline $KMnO_4$ solution; the *o*-xylene will suffer side-chain oxidation and decolorise the permanganate solution. Or warm a few drops of the sample in conc. H_2SO_4; the *o*-xylene will undergo sulfonation and the product is soluble in sulfuric acid so that the sample forms a homogeneous solution.

4. 

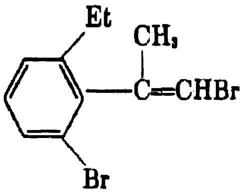
5. Oxidise the samples with alk. $KMnO_4$ aq. to the respective dicarboxylic acids and take the melting points of the products. These m.p.'s differ sufficiently (ortho, 231°; meta, 348°; para, 300°) to permit identification of the di-acids.

6. $C_6H_5CH_3 \xrightarrow{\text{[illegible]}} C_6H_5CO_2H \xrightarrow{NaOH} C_6H_5CO_2Na \xrightarrow[\Delta]{NaOH,\ CaO} C_6H_6$.

7. (a) Cl_2, Fe, (b) C_2H_5Br + Na, (c) permanganate oxidation, (d) $HNO_3—H_2SO_4$.

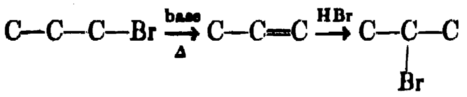
8. Only *c* is optically active, since its mirror images are not superposable; *a* and *b* have symmetrical rings, which permits the mirror images to "fit" the same mold.

9. Yes, steric hindrance prevents rotation about the $C_{ar}—C_{\alpha}$ bond and the methyl group gets "locked" on either side of the phenyl ring. The two isomers are nonsuperposable, which gives rise to optical isomerism.



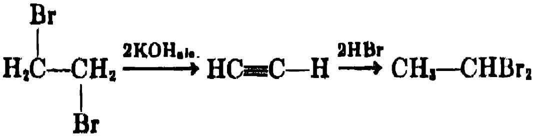
10. Of the three Kekulé structures for naphthalene, the $C_1—C_2$ bond is a double bond in two and a single bond in one, whereas the $C_2—C_3$ bond is a single bond in two and a double bond in one. Thus, the $C_1—C_2$ bond has a greater resemblance to a double bond than the $C_2—C_3$ bond.

Set 9 (page 246)

1. 

$$C—C—C—Br \xrightarrow[\Delta]{base} C—C{=}C \xrightarrow{HBr} C—\underset{\displaystyle Br}{\underset{|}{C}}—C$$

2. Chlorides are cheaper to produce, chlorine being less costly than bromine, and also, chlorides are less reactive and more stable in air and sunlight than bromides and iodides, particularly the latter.

3. 

$$H_2\overset{\displaystyle Br}{\overset{|}{C}}—\underset{\displaystyle Br}{\underset{|}{CH_2}} \xrightarrow{2KOH_{alc.}} HC{\equiv}C—H \xrightarrow{2HBr} CH_3—CHBr_2$$

4. 4.48 liters.

5. (a) Test for unsaturation with dil. $KMnO_4$ aq. or Br_2/CCl_4, or test for ease of hydrolysis with $AgNO_3$ aq.; (b) test for ease of hydrolysis with aq. $AgNO_3$ at room temperature; (c) test for ease of hydrolysis with aq. $AgNO_3$, the $CH_2{=}CH—CH_2Br$ gives a precipitate at room temperature; (d) the unsaturated compound will decolorise dil. aq. $KMnO_4$ or Br_2/CCl_4 solutions rapidly at room temperature.

6. 100 ml.

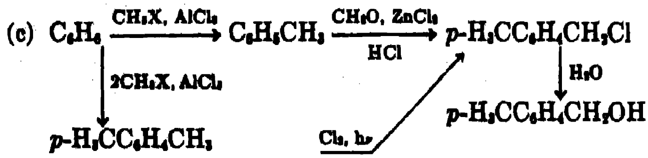
7. Since the dipole which arises from the resonance

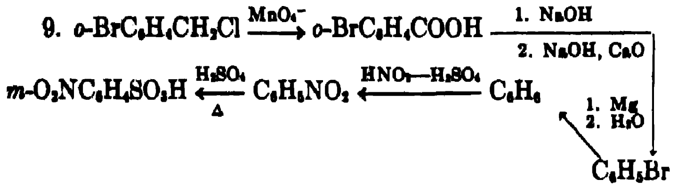
$$CH_2{=}CH—Cl,\quad {}^{-}CH_2—CH{=}\overset{+}{Cl}$$

is in the opposite direction to that from induction (the effect of differences in electronegativity), the observed dipole moment of vinyl chloride is less than that of CH_3CH_2Cl, where only the inductive effect operates.

8. (a) $C_6H_6 \xrightarrow[AlCl_3]{CH_3Br} C_6H_5CH_3 \xrightarrow{MnO_4^-} C_6H_5\,COOH \xrightarrow{Br_2,\ Fe} m\text{-}BrC_6H_4COOH$

(b) $C_6H_6 \xrightarrow{HNO_3,\ H_2SO_4} C_6H_5NO_2 \xrightarrow{Cl_2,\ Fe} m\text{-}ClC_6H_4NO_2$

(c) 

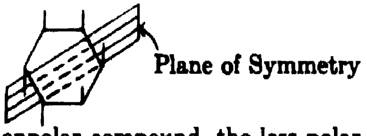
9. 

10. (a) 1-Chloro-4-methylcyclohexane would form a precipitate when gently warmed with aq. $AgNO_3$, *p*-chlorotoluene would not; or, *p*-chlorotoluene would form a yellow product when warmed with conc. HNO_3, the cyclohexyl compound would not.

(b) The toluene would be oxidized by aq. $KMnO_4$ when boiled a few minutes, and the purple color of the reagent would be replaced by an almost black precipitate; or, the chlorobenzene would react with magnesium in dry ether and the magnesium would mostly disappear; or, fuse the sample with sodium metal, cool, acidify, and add Ag^+, the chloro compound would give a precipitate of AgCl.

(c) Benzene hexachloride would hydrolyze enough in boiling water to give a precipitate with Ag^+.

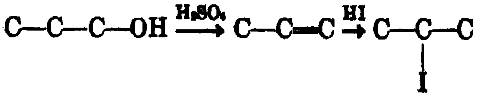
11. No. No.



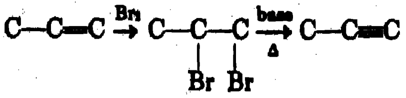
12. Since *p*-dichlorobenzene is a nonpolar compound, the less polar the liquid the better solvent it will be for *p*-dichlorobenzene. The alcohol with the larger hydrocarbon fragment is the less polar; hence, n-propyl alcohol would be the better solvent.

Set 10 (page 292)

1. Test for the OH group in the alcohol by dissolving it in an ether or hydrocarbon solvent and using ceric ammonium nitrate reagent or sodium metal. Sodium would form the white, insoluble alkoxide, whereas the ceric reagent would turn red.

2. (a) 
$C—C—C—OH \xrightarrow{H_2SO_4} C—C{=}C \xrightarrow{HI} C—\underset{\displaystyle I}{\underset{|}{C}}—C$

(b) $C—C—C—OH \xrightarrow{PX_3} C—C—C—X \xrightarrow{2Na} C—C—C—C—C—C$

(c) 
$C—C{=}C \xrightarrow{Br_2} C—\underset{\displaystyle Br}{\underset{|}{C}}—\underset{\displaystyle Br}{\underset{|}{C}} \xrightarrow[\Delta]{base} C—C{\equiv}C$

(d) $C—C—C—X \xrightarrow[\text{2. } H_2CO]{\text{1. Mg}} C—C—C—C—OH$

3. 255 liters; 3730 liters.

4. Because oxidation tends to take place where oxidation has already begun, i.e., C—OH carbon

5. No, it would form a solvate. Use anhyd. Na_2SO_4 preferably, but BaO or K_2CO_3 will serve.

6. 0.701 liters; 0.488 liters.

7. It is associated and behaves as aggregates of H_2O (M.W. = 18) or $(H_2O)_x$.

8. (a) Treat a sample with excess Na and measure the volume of hydrogen gas evolved. (b) As in (a); or, measure the volume of cold, standardized Br_2/CCl_4 solution decolorized by a sample to calculate the quantity of *n*-hexene present.

9. (a) Use sodium metal or ceric ammonium nitrate to test for the OH groups as in problem under 1. (b) Sodium propoxide is very soluble in pure alcohol, sodium hydroxide is not. (c) Use the periodic acid test for a 1,2-glycol; only the 1,2-pentanediol gives a positive test. (d) Use the Lucas test; isobutyl alcohol is a primary alcohol, isopropyl alcohol is a secondary alcohol. (e) Test for unsaturation with dilute permanganate solution.

10. 46; 92.

11. $40H^+ + 5Cr_2O_7^{=} + 3CH_3CH_2CH{=}CH_2 \rightarrow 10Cr^{+3}\ 23H_2O$

$$+ 3CO_2 + 3CH_3CH_2CO_2H.$$

12. 199 g.

13. 9.2%.

14. $C_5H_{12}O_2$.

15. 107 g.

16. (a) $5CH_3—CH_2—C(\overset{+}{N}H_3){=}CH—CHOH—CO—COOH + 50H^+ + 17MnO_4^-$

$$\rightarrow 17Mn^{+2} + 38H_2O + 5CH_3—CH_2CO_2H + 5/2\ N_2 + 20\ CO_2$$

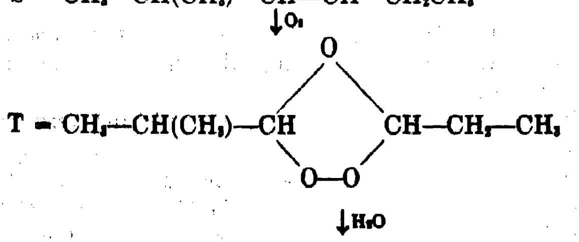
(b) $3CH_3CH_2C(NH_2){=}CH—CHOH—CO—CO_2^- \rightarrow 3CH_3CH_2CO_2^- + 3/2\ N_2$

$$+ 7(OH^-) + 17MnO_4^- + 12CO_3^{=} + 11H_2O$$

$$+ 17MnO_2$$

17. S = $CH_3—CH(CH_3)—CH{=}CH—CH_2CH_3$

T =



$CH_3—CH(CH_3)—CH{=}O + O{=}CH—CH_2—CH_3$

18. $CH_3—CH_2—CHO + CH_3CH_2MgBr \xrightarrow{\text{then } H_3O^+}$ 3-Pentanol

17.6 g = 0.2 mole

0.2 mole C_2H_5Br = 21.8 g

19. The empirical formula and the lack of unsaturation indicate one ring in X. The IR bands show the presence of an OH group (secondary OH region) and absence of a carbonyl group. Oxidation occurs without loss of carbon to produce two acid groups; hence oxidation must have opened a ring. Possible structures: cycloheptanol, a methylcyclohexanol (2-methyl, 3-methyl, etc.), a dimethylcyclopentanol, etc.

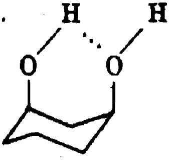
20. MeOH: EtOH: $CH_2OH—CH_2OH$ = 46:60:62.

21. On a basis of their molecular weights; H_2O boils at a much higher temperature owing to association through intermolecular hydrogen bonding.

22. (a) 2-Hexene, (b) 2-Methyl-2-hexene, (c) 2-methyl-3-hexene, (d) 3-methyl-2-hexene.

23. No, the residue. The 95% azeotrope boils at the lower temperature to produce the distillate.

24. Diethyl sulfide does not form hydrogen bonds and the S—H···S bonds of ethanethiol are too weak to give a measurable association. Therefore the sulfide has the higher boiling point because of its larger molecular weight. Ethyl alcohol is associated, whereas ethyl ether is not, and the association factor outweighs the larger molecular weight of the ether to give the alcohol the higher boiling point.

25. 

Largely monomeric; 1,4 and 1,2 isomers associated.

26. Note the formation of color when a de-aerated tube is heated; or note the freezing point decrease when the de-aerated tube is chilled.

27. The phenol would give the $FeCl_3$ color test, the carbinol would not; or, the carbinol will give a red color in H_2SO_4, the phenol would not.

28. Salt of a weak acid is basic, and the weaker the acid the more basic is the salt. Hence, the phenoxide will be the more basic or have the higher *p*H.

29. (a) Phenol gives color with aq. $FeCl_3$. (b) Phenol gives color with aq. $FeCl_3$. (c) Picric acid soluble in water (strong acid), phenol not very soluble in water at room temperature; or, picric acid forms a precipitate (molecular addition compound) in $CHCl_3$ solution with most amines, phenol will not. (d) 3,5-Dimethylphenol, with ring positions ortho and para to the OH open, will react instantaneously with bromine to give a precipitate (the tribromo derivative), the 2,4,6-trimethylphenol will react but not so rapidly.

30. 87.3 g.

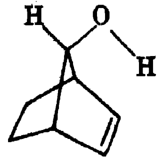
31. The *t*-butyl groups shield the OH from the base and from the ferric ion to prevent reaction, whereas the methyl groups in the dimethylphenol are not so large as to block the approach of the reagents.

32. CCl_4 is the least soluble, because it is a nonpolar molecule and very slightly soluble in a polar liquid like water. The three electronegative halogen atoms in $CHCl_3$ and $CHBr_3$ increase the electronegativity of the carbon, which gives the C—H bond sufficient polarity to produce some hydrogen bonding of the C—H bond with water molecules. This is not large but does produce an increase in the solubilities of these haloforms in water, which is a hundredfold in the case of $CHCl_3$ compared to CCl_4. Since Cl is more electronegative than Br, the effect is larger for $CHCl_3$ than for $CHBr_3$.

33. There is an intramolecular hydrogen bond in salicylaldehyde which lowers ν_{CO} as well as ν_{OH}.

34. An intramolecular hydrogen bond can be formed when the OH is *syn* to the double bond. This decreases $\nu_{O—H}$ as observed for III and IV. Hence, structure I must

have structure Ib. If structure I were hydrogenated, its ν_{OH} should be near that of II. Experimentally it is found to be 3618 cm^{-1}.



35. One could measure the infrared absorption ν_{OH} frequencies and the proton n.m.r. spectra in the $\tau = 3.8$–5.4 range. R and S would exhibit τ values in the vinyl proton range, whereas T would not (which identifies T), and S would exhibit ν_{OH} about 50 cm^{-1} lower than R. Or, S is distinguished by ν_{OH} from R and T (ν_{OH} for S lower than that of R and T), and then R and T are distinguished by the n.m.r. τ values.

Set 11 (page 302)

1. If a symmetrical ether were linear, it would have no dipole moment, for then the moments of the C—O bonds would cancel each other.

2. It dissolves in water and in ether by forming oxonium ions with the solvent. It is much more soluble in the water because the large dielectric constant of water enables it to support ions, in which case the $H_3\overset{+}{O}\overset{-}{Cl}$ ion pairs separate (ionize). HCl does not react with *n*-hexane or CCl_4, and since HCl is a polar molecule, it does not dissolve in the nonpolar solvents.

3. *n*-Heptane.

4. Ethers form a solvate with the Grignard agent through the basic oxygen atom of the ethers. Alkanes cannot do this. No, because a Grignard reagent would immediately react with the alcohol solvent.

5. Dioxane, b.p. 101°; 1,4-thioxane, b.p. 150°.

Set 12 (page 333)

1. A test for water solubility would identify acetone. Test with 2,4-dinitrophenylhydrazine to identify the aldehyde or ceric ammonium nitrate to identify the alcohol; (b) Tollens' reagent to identify the aldehyde or iodoform test to detect the methyl ketone; (c) the iodoform test will identify the 2-hexanol; (d) acetone is water soluble, the other is not; (e) the iodoform test will identify the 2-bromohexane.

3. 90%.

4. (a) $3C_5H_{11}CHO + 2MnO_4^- + OH^- \rightarrow 3C_5H_{11}CO_2^- + 2MnO_2 + 2H_2O$
   (b) $8H^+ + 3C_6H_{14}O + Cr_2O_7^{=} \rightarrow 3C_6H_{12}O + 2Cr^{+3} + 7H_2O$

5. Molecular formula $C_5H_{10}O$, no aldehyde, methyl ketone; hence 2-pentanone or isopropyl methyl ketone.

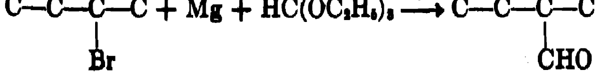
6. Empirical formula $(C_3H_8O)_n$, MW = 60 or a multiple of 60.

7. Iodoform test positive for ethyl alcohol.

8. (a) Dissolve the acetone in water and recover by distillation; form sodium bisulfite addition compound of hexanal, filter, and recover heptane from filtrate as an insoluble liquid layer; regenerate hexanal with acid.
   (b) Extract ethylene glycol with water and distill off the water; isolate aldehyde through its sodium bisulfite addition compound.

9. 32.4 g.

10.

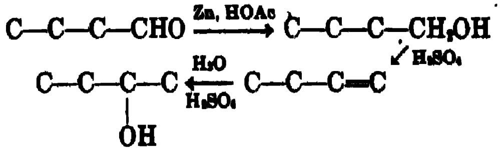


$$C{-}C{-}\underset{\displaystyle Br}{\underset{|}{C}}{-}C + Mg + HC(OC_2H_5)_3 \xrightarrow[\text{then}]{} \xrightarrow{H_3O^+} C{-}C{-}\underset{\displaystyle CHO}{\underset{|}{C}}{-}C$$

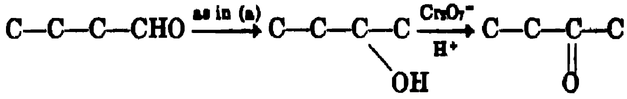
17.2 = 0.2 mole product; hence, need 0.2 mole.
2-bromobutane = 27.4 g, plus 0.2 mole $HC(OC_2H_5)_3$ = 29.6 g.

11. 36%.

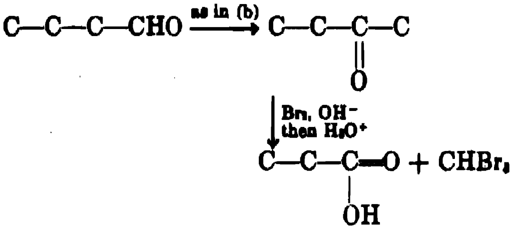
12. (a)



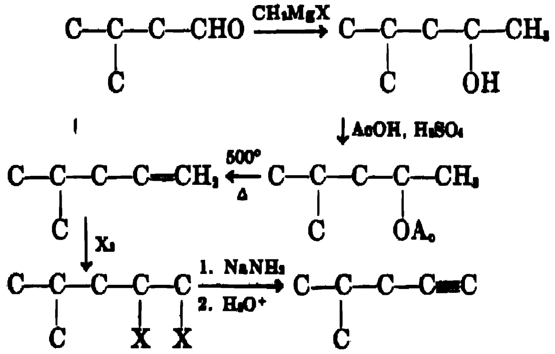
(b)



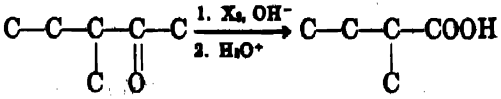
(c)



13. (a)



(b)



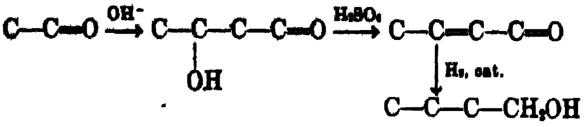
14. Use Tollens' reagent to oxidize the CHO to a COOH group, or $\phi CHO \xrightarrow{H_2NOH} \phi CH{=}NOH \xrightarrow{Ac_2O} \phi CN \xrightarrow[\Delta]{H_3O^+} \phi CO_2H$

15. The benzaldehyde undergoes autooxidation to produce ϕ—CO_2H which then oxidizes the other substance.

16. (a) Remove ϕCHO via its sodium bisulfite addition compound and regenerate with dilute acid, extract the ϕCO_2H from the ϕNO_2 with dil. aq. NaOH and regenerate with acid. (b) Extract the salicylaldehyde and *p*-nitrophenol with dil. NaOH, regenerate with acid, and separate these two compounds by steam distillation or through the sodium bisulfite addition compound of the aldehyde. The *p*-bromobenzaldehyde can be separated from the ketone via the sodium bisulfite addition compound of the aldehyde.

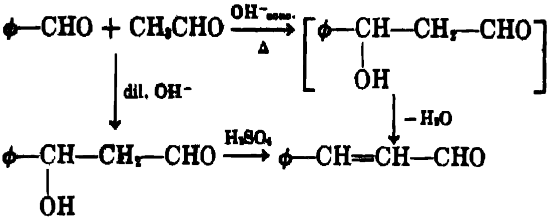
17. 180 g.

18. (a)



$$\mathrm{C{-}C{=}O \xrightarrow{OH^-} C{-}\underset{OH}{C}{-}C{-}C{=}O \xrightarrow{H_2SO_4} C{-}C{=}C{-}C{=}O \xrightarrow{H_2,\ cat.} C{-}C{-}C{-}CH_2OH}$$

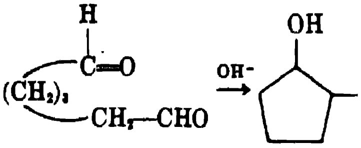
(b)



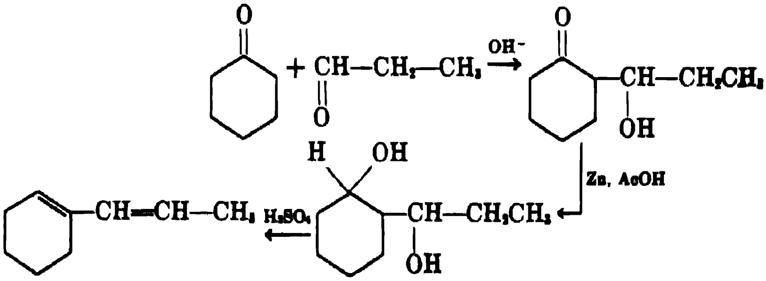
$$\mathrm{\phi{-}CHO + CH_3CHO \xrightarrow[\Delta]{OH^-\ conc.} \left[\phi{-}\underset{OH}{CH}{-}CH_2{-}CHO\right] \xrightarrow{-H_2O} \phi{-}CH{=}CH{-}CHO}$$

$$\mathrm{\phi{-}CHO + CH_3CHO \xrightarrow{dil.\ OH^-} \phi{-}\underset{OH}{CH}{-}CH_2{-}CHO \xrightarrow{H_2SO_4} \phi{-}CH{=}CH{-}CHO}$$

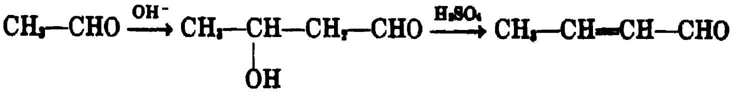
(c)



(d)



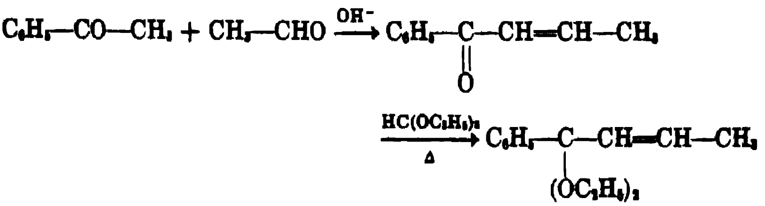
(e)



$$\mathrm{CH_3{-}CHO \xrightarrow{OH^-} CH_3{-}\underset{OH}{CH}{-}CH_2{-}CHO \xrightarrow{H_2SO_4} CH_3{-}CH{=}CH{-}CHO}$$

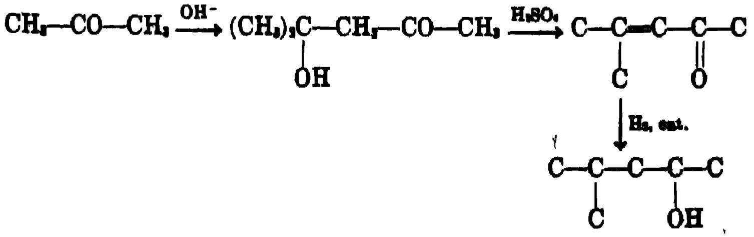
(f) $\mathrm{CH_3{-}CHO + 3H_2C{=}O \xrightarrow{OH^-} (HOCH_2)_3{-}C{-}CHO \xrightarrow{NaHg} (HOCH_2)_4{-}C}$

(g)



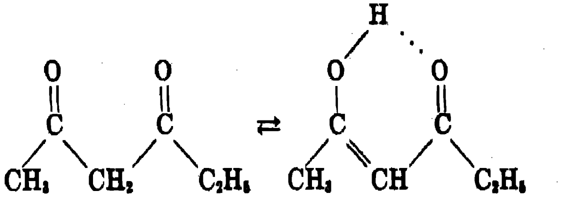
$$\mathrm{C_6H_5{-}CO{-}CH_3 + CH_3{-}CHO \xrightarrow{OH^-} C_6H_5{-}\underset{\|O}{C}{-}CH{=}CH{-}CH_3 \xrightarrow[\Delta]{HC(OC_2H_5)_3} C_6H_5{-}\underset{(OC_2H_5)_2}{C}{-}CH{=}CH{-}CH_3}$$

(h)



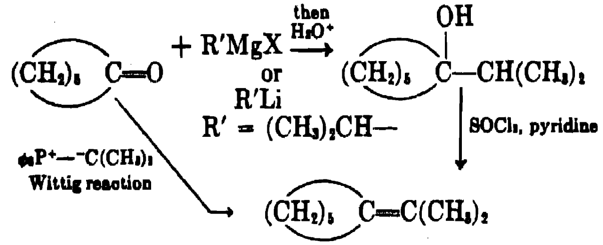
$$\mathrm{CH_3{-}CO{-}CH_3 \xrightarrow{OH^-} (CH_3)_2\underset{OH}{C}{-}CH_2{-}CO{-}CH_3 \xrightarrow{H_2SO_4} C{-}\underset{C}{C}{=}C{-}\underset{\|O}{C}{-}C \xrightarrow{H_2,\ cat.} C{-}\underset{C}{C}{-}C{-}\underset{OH}{C}{-}C}$$

20. The 2,4-isomer has the larger enol content because the enol can form an intramolecular hydrogen bond involving a six-membered ring.



The hydrogen bond stabilizes the enol and shifts the equilibrium toward greater enol content. The 2,5-isomer could only form such a bond with a seven-membered ring, but such rings are not very stable, and therefore the more stable diketone tautomer greatly predominates.

21. Two good routes are as follows:



22. Bond angle strain in the C_3 ring is partially reduced by forming the hydrate in which the carbonyl changes from sp^2 to sp^3 hybridization.

23. Benzoylacetone is largely enolic. The strong intramolecular hydrogen bond produces the substantial lowering of the $\nu_{C=O}$ and ν_{O-H} frequencies.

24. A has structure II and B has structure III.

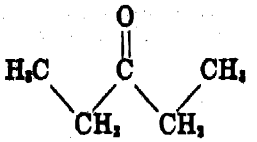
A: UV indicates C=C—C=O; ν = 1714 cm^{-1} (top C=O), 1670 cm^{-1} (conj. C=O), 1624 cm^{-1} (C=C), 987 cm^{-1} (*trans* C=C); n.m.r. doublet (coupling of a vinyl proton with β vinyl proton) and sextet (coupling of B vinyl proton with methylene H's, and each split by coupling with α vinyl proton).

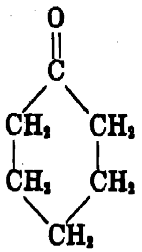
B: Isolated C=O has λ_m below 200 mμ (except for low band near 280 mμ of $\epsilon < 50$); ν = 1718 cm^{-1} (isolated C=O) and 971 cm^{-1} (*trans* C=C).

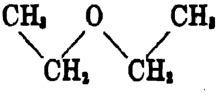
25. R: 1720 cm^{-1} (C=O). S: 1680 cm^{-1} (conj. C=O); λ_m = 224 mμ (C=C—C=O). T: 3570 and 3470 cm^{-1} (H-bonded OH groups), 1715 cm^{-1} (C=O). V: 1770 cm^{-1} (ester C=O), 1700 cm^{-1} (conj. C=O), 1655 cm^{-1} (conj. C=C).

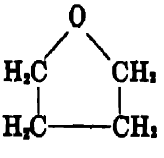
26. $(CH_2{=}CH)_2C{=}O$.

27. Steric hindrance by the ethyl groups of diethyl ketone prevents the bisulfite ion from reaching the carbonyl carbon atom, whereas in cyclohexanone, the carbon chains are held back. It is similar to the case of ethyl ether and tetrahydrofuran, in which the former is very slightly soluble in water but the cyclic ether is completely soluble. Also, the trigonal carbon of cyclohexanone produces some ring strain, which is relieved by the addition of the bisulfite to form a tetrahedral carbon atom.



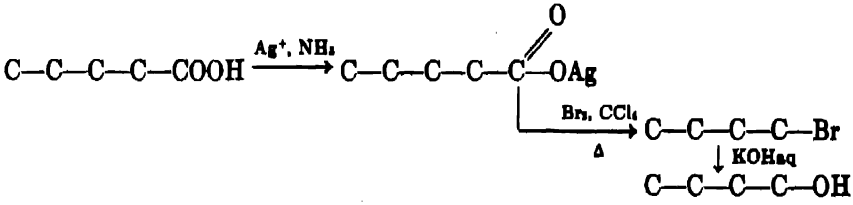






Set 13 (page 358)

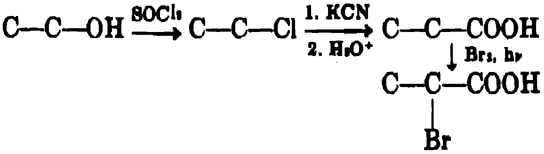
1. 6.43 g.

2. 

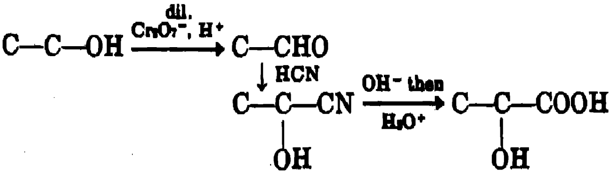
$$C—C—C—C—COOH \xrightarrow{Ag^+,\ NH_3} C—C—C—C—\overset{O}{\overset{\|}{C}}—OAg \xrightarrow[\Delta]{Br_2,\ CCl_4} C—C—C—C—Br \xrightarrow{KOH_{aq}} C—C—C—C—OH$$

3. $C—C—C—C—OH \xrightarrow{PBr_3} C—C—C—C—Br \xrightarrow[\text{or } Mg,\ CO_2,\ \text{then } H_3O^+]{1.\ KCN\quad 2.\ H_3O^+} C—C—C—C—COOH$

4. 41.6 ml.
5. 116.
6. Heat with MnO and conduct any gas formed into lime water; any formic acid present would yield CO_2, which would form a white precipitate in the lime water. Or, treat a sample with Tollens' reagent; any formic acid present would produce silver.

7. (a) 

$$C—C—OH \xrightarrow{SOCl_2} C—C—Cl \xrightarrow[2.\ H_3O^+]{1.\ KCN} C—C—COOH \xrightarrow{Br_2,\ h\nu} C—\underset{Br}{\underset{|}{C}}—COOH$$

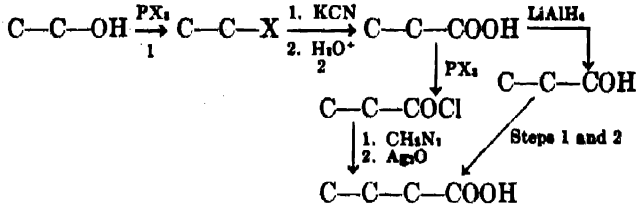
(b) 

$$C—C—OH \xrightarrow{\text{dil. } Cr_2O_7^{=},\ H^+} C—CHO \xrightarrow{HCN} C—\underset{OH}{\underset{|}{C}}—CN \xrightarrow[H_3O^+]{OH^-\ \text{then}} C—\underset{OH}{\underset{|}{C}}—COOH$$

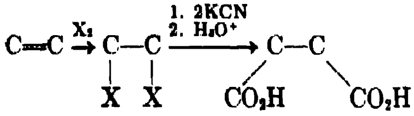
8. No. Less soluble, owing to ionic strengths of the saturated solution ("salting out" effect). The organic acid more soluble in aq. K_2CO_3 because the acid forms a soluble salt.

9. (a) $C{-}OH \xrightarrow{PX_3} C{-}X \xrightarrow[\text{then } H_3O^+]{Mg,\ CO_2} C{-}COOH \xrightarrow{3Cl_2,\ P} CCl_3{-}COOH$

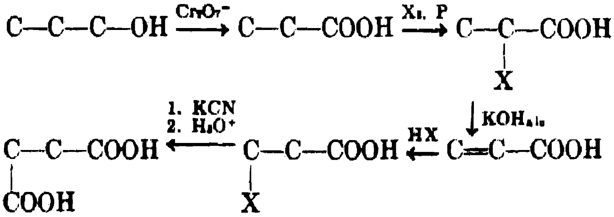
(b)



(c)



(d)

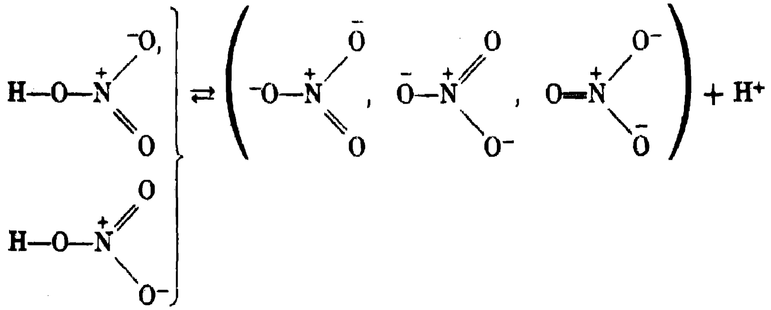


10. Heat and pass any gas generated into lime water. A precipitate ($CaCO_3$) would indicate the evolution of CO_2 from oxalic acid; hence, oxalic acid would contain carbon.

11. 7.03 g; the same, two equivalents per mole.

12. (a) Heat the sample; oxalic acid yields CO_2, which will give a white precipitate with lime water. Incidentally, one is a solid, one a liquid. (b) Heat the sample; malonic acid would evolve CO_2 and form a precipitate with lime water.

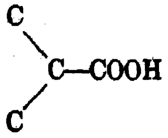
13.



$$\begin{pmatrix} H{-}O{-}N{=}O, \\ H{-}O{-}\overset{+}{N}{-}O^- \end{pmatrix} \rightleftarrows (^-O{-}N{=}O,\ O{=}N{-}O^-) + H^+$$

The resonance stabilization of the nitrate ion is greater than it is for the nitrite ion, which favors ionization of the former.

14.



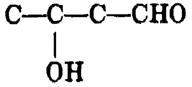
15. Relative electronegativities of Cl, H and CH_3 decrease in that order. Hence, the inductive effect in CCl_3COOH, CH_3COOH, and $(CH_3)_3C—COOH$ decreases the acid strength of these acids in the order given. On this basis, relative acid strengths would be (a) $Cl—CH_2COOH > Br—CH_2COOH$; (b) $CH_3—CHCl—COOH > Cl—CH_2—CH_2COOH$.

16. Reduces Tollens' reagent; therefore CHO.

$Na \rightarrow H_2$; therefore active H, probably OH.

Iodoform; therefore $CO—CH_3$ or $CHOH—CH_3$. Cannot be the ketone, since it would have only two oxygen atoms and has already used two for CHO and OH groups.

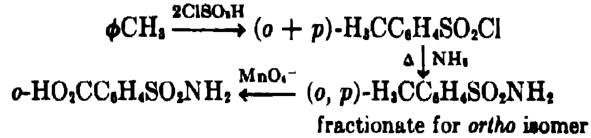
Ans.:



$$C—\underset{\underset{OH}{|}}{C}—C—CHO$$

17. 294 g.

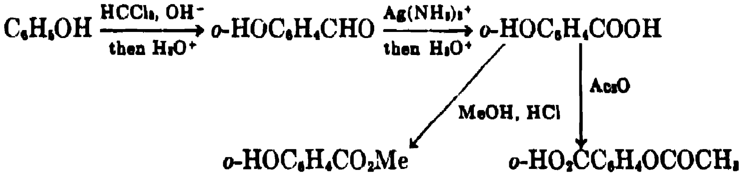
18.



$$\begin{tikzcd}
 & \phi CH_3 \arrow[r, "2ClSO_3H"] & (o+p)\text{-}H_3CC_6H_4SO_2Cl \arrow[d, "\Delta", "NH_3"'] \\
 & o\text{-}HO_2CC_6H_4SO_2NH_2 & (o,\ p)\text{-}H_3CC_6H_4SO_2NH_2 \arrow[l, "MnO_4^-"']
\end{tikzcd}$$

fractionate for *ortho* isomer

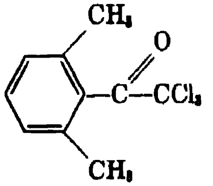
19.



$$\begin{tikzcd}
C_6H_5OH \arrow[r, "HCCl_3,\ OH^-", "then\ H_3O^+"'] & o\text{-}HOC_6H_4CHO \arrow[r, "Ag(NH_3)_2^+", "then\ H_3O^+"'] & o\text{-}HOC_6H_4COOH \arrow[dl, "MeOH,\ HCl"] \arrow[d, "Ac_2O"] \\
 & o\text{-}HOC_6H_4CO_2Me & o\text{-}HO_2CC_6H_4OCOCH_3
\end{tikzcd}$$

20. Ethyl ether is more polar than petroleum ether and should make the better solvent for the polar benzoic acid.

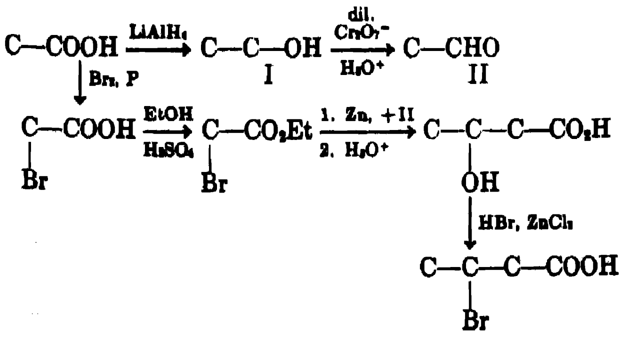
21. The methyl groups and the CCl_3 group in



block the approach of H_2O molecules or of OH^- ions from attacking the C═O group for hydrolysis.

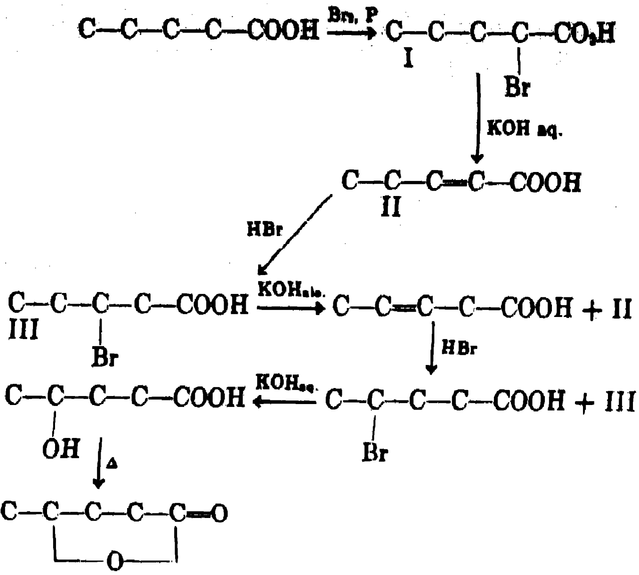
22. (a) Test for unsaturation; (b) test for formation of acetylide with ammoniacal cuprous ion.

23.

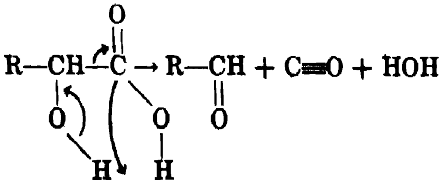


$$\begin{tikzcd}
C—COOH \arrow[r, "LiAlH_4"] \arrow[d, "Br_2,\ P"] & \underset{I}{C—C—OH} \arrow[r, "dil.\ Cr_2O_7^{2-}", "H_3O^+"'] & \underset{II}{C—CHO} \\
\underset{\underset{Br}{|}}{C}—COOH \arrow[r, "EtOH", "H_2SO_4"'] & \underset{\underset{Br}{|}}{C}—CO_2Et \arrow[r, "1.\ Zn,\ +II", "2.\ H_3O^+"'] & C—\underset{\underset{OH}{|}}{C}—C—CO_2H \arrow[d, "HBr,\ ZnCl_2"] \\
 & & C—\underset{\underset{Br}{|}}{C}—C—COOH
\end{tikzcd}$$

(b)

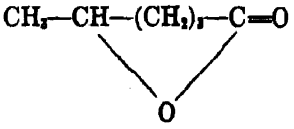


24.



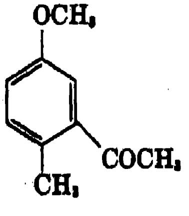
25. Compound I should have a single methylenic peak, whereas II should have two —one a doublet and one a singlet. Also, II should have a $>$C—H triplet peak. Found: I, T = 6.31 (s) II, τ = 5.45 (t) ($>$C—H); τ = 6.47 (s) and 6.94 (d). Since the COOH groups are fairly close together in II, K_2 is markedly reduced by the ionization of the first carboxyl group, whereas in II the two groups act more or less independently and have K's in the same order of magnitude. Found: I, K_1 and K_2 = 1.23 × 10^{-4} and 1.95 × 10^{-7}, respectively; II, K_1 and K_2 = 7.25 × 10^{-6} and 1.23 × 10^{-5}, respectively.

26.



CH_3—CH—$(CH_2)_3$—C=O (—O—)

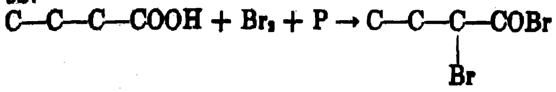
27.



Set 14 (page 368)

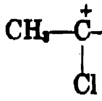
1. Acetyl bromide would hydrolyze in cold water and give a precipitate with Ag^+ very quickly; bromoacetic acid would react much more slowly.

2. 92.

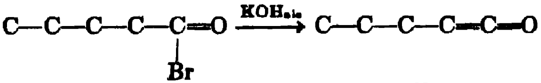
3. 

$$C—C—C—COOH + Br_2 + P \rightarrow C—C—\underset{\displaystyle Br}{\underset{|}{C}}—COBr$$

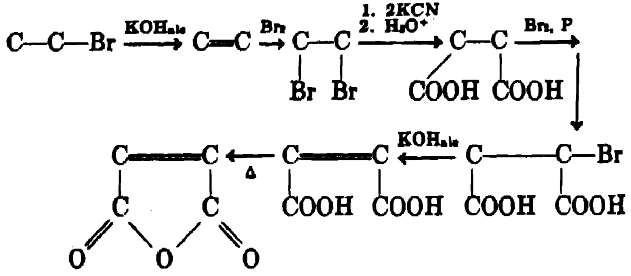
4. The polar character of the carbonyl bond $CH_3—\underset{\displaystyle Cl}{\underset{|}{\overset{+}{C}}}—O^-$ facilitates reaction with a nucleophilic reagent.

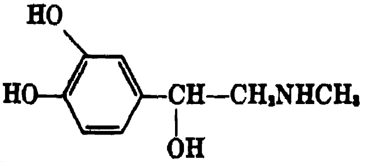


5. Titrate the mixture in ice water very rapidly to determine the acetic acid content. After an initial run is made, one can make a second run using the calculated volume of base required within a few drops; then quickly titrate to the end point.

6. 

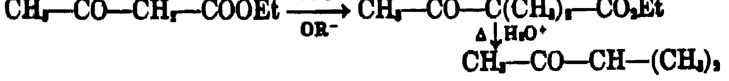
$$C—C—C—\underset{\displaystyle Br}{\underset{|}{C}}—C{=}O \xrightarrow{KOH_{alc}} C—C—C—C{=}C{=}O$$

7. 

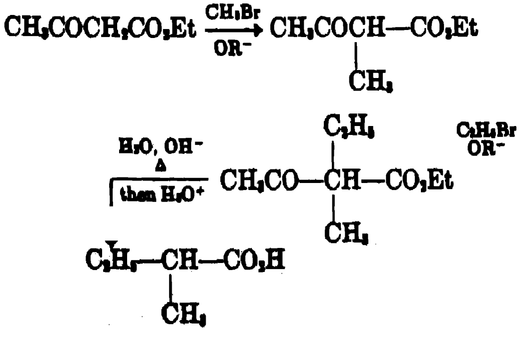
8. 

Set 15 (page 393)

1. 20¢.

2. (a) 

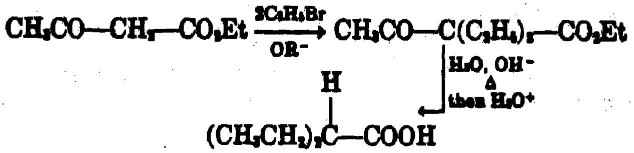
$$CH_3—CO—CH_2—COOEt \xrightarrow[OR^-]{2CH_3Br} CH_3—CO—C(CH_3)_2—CO_2Et$$
$$\downarrow \Delta,\ H_3O^+$$
$$CH_3—CO—CH—(CH_3)_2$$

(b) 

$$CH_3COCH_2CO_2Et \xrightarrow[OR^-]{CH_3Br} CH_3CO\underset{\displaystyle CH_3}{\underset{|}{C}}H—CO_2Et \xrightarrow[OR^-]{C_2H_5Br} CH_3CO—\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle C_2H_5}{\overset{|}{C}}}}—CO_2Et$$

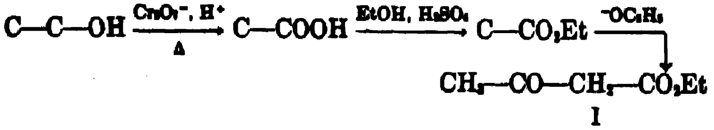
$$\xrightarrow[\text{then } H_3O^+]{H_2O,\ OH^-,\ \Delta} C_2H_5—\underset{\displaystyle CH_3}{\underset{|}{C}}H—CO_2H$$

(c)

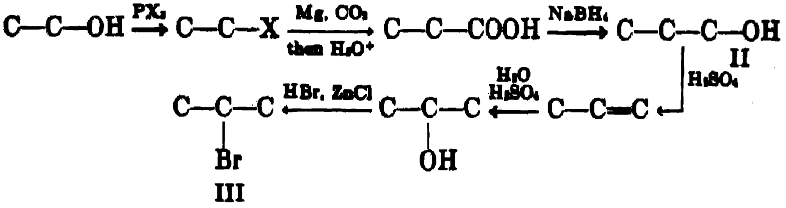


$CH_3CO{-}CH_2{-}CO_2Et \xrightarrow[OR^-]{2C_2H_5Br} CH_3CO{-}C(C_2H_5)_2{-}CO_2Et \xrightarrow[\text{then } H_3O^+]{H_2O,\ OH^-,\ \Delta} (CH_3CH_2)_2\overset{H}{C}{-}COOH$

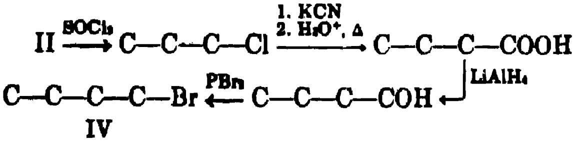
3.



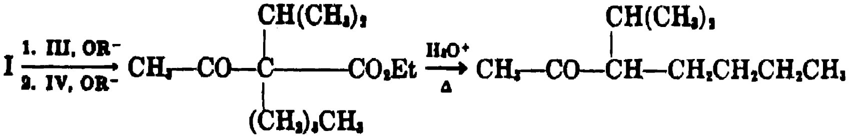
$C{-}C{-}OH \xrightarrow[\Delta]{Cr_2O_7^{=},\ H^+} C{-}COOH \xrightarrow{EtOH,\ H_2SO_4} C{-}CO_2Et \xrightarrow{^-OC_2H_5} \underset{\text{I}}{CH_3{-}CO{-}CH_2{-}CO_2Et}$



$C{-}C{-}OH \xrightarrow{PX_3} C{-}C{-}X \xrightarrow[\text{then } H_3O^+]{Mg,\ CO_2} C{-}C{-}COOH \xrightarrow{NaBH_4} \underset{\text{II}}{C{-}C{-}C{-}OH} \xrightarrow{H_2SO_4} C{-}C{=}C \xrightarrow{H_2O,\ H_2SO_4} C{-}\underset{OH}{C}{-}C \xrightarrow{HBr,\ ZnCl_2} \underset{\text{III}}{C{-}\underset{Br}{C}{-}C}$

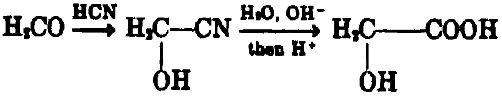


$\text{II} \xrightarrow{SOCl_2} C{-}C{-}C{-}Cl \xrightarrow[2.\ H_3O^+,\ \Delta]{1.\ KCN} C{-}C{-}C{-}COOH \xrightarrow{LiAlH_4} C{-}C{-}C{-}COH \xrightarrow{PBr_3} \underset{\text{IV}}{C{-}C{-}C{-}C{-}Br}$



$\text{I} \xrightarrow[2.\ \text{IV},\ OR^-]{1.\ \text{III},\ OR^-} CH_3{-}CO{-}\overset{CH(CH_3)_2}{\underset{(CH_2)_3CH_3}{C}}{-}CO_2Et \xrightarrow[\Delta]{H_3O^+} CH_3{-}CO{-}\overset{CH(CH_3)_2}{CH}{-}CH_2CH_2CH_2CH_3$

4.



$H_2CO \xrightarrow{HCN} H_2\underset{OH}{C}{-}CN \xrightarrow[\text{then } H^+]{H_2O,\ OH^-} H_2\underset{OH}{C}{-}COOH$

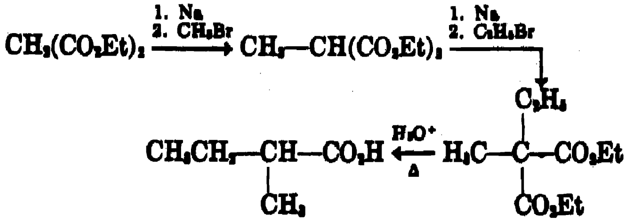
5. (a) Ethyl α-methylacetoacetate will enolize and dissolve in aq. NaOH; the α,α-dimethyl ester will not.

   (b) a mineral oil is a hydrocarbon; a vegetable oil is a glyceride. The latter will hydrolyze in aq. NaOH and then dissolve when diluted; the mineral oil will not.

6. 244 g.

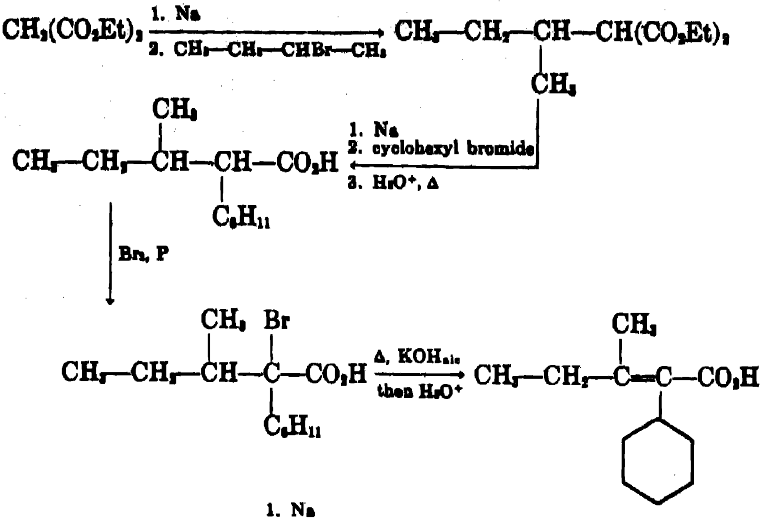
7. 1.57 moles.

8. (a)

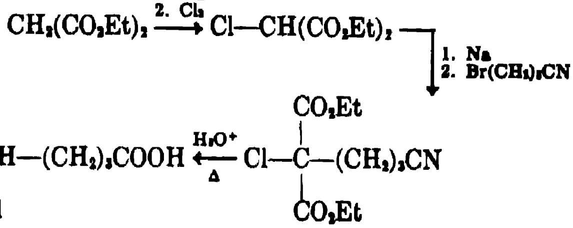


$CH_2(CO_2Et)_2 \xrightarrow[2.\ CH_3Br]{1.\ Na} CH_3{-}CH(CO_2Et)_2 \xrightarrow[2.\ C_2H_5Br]{1.\ Na} H_3C{-}\overset{C_2H_5}{\underset{CO_2Et}{C}}{-}CO_2Et \xrightarrow[\Delta]{H_3O^+} CH_3CH_2{-}\underset{CH_3}{CH}{-}CO_2H$

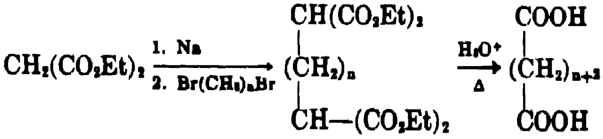
(b)



(c)

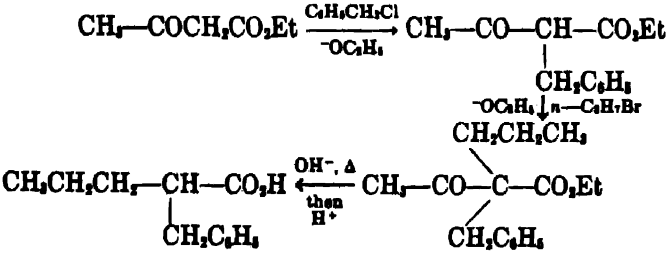


(d)

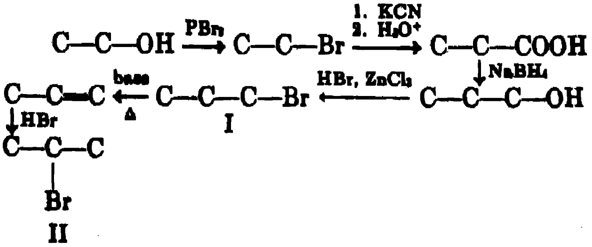


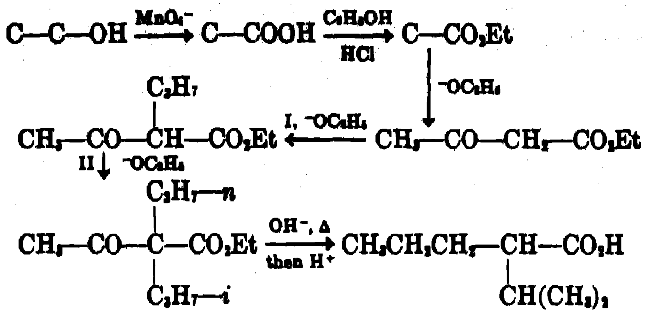
n = 1 for glutaric acid
n = 2 for adipic acid

(e)



(f)





9. 96.2 g, if two steps are used.

10. By taking two aliquots of the same material and testing one for an enol with aq. $FeCl_3$ and the other for a ketone with 2,4-dinitrophenylhydrazine reagent.

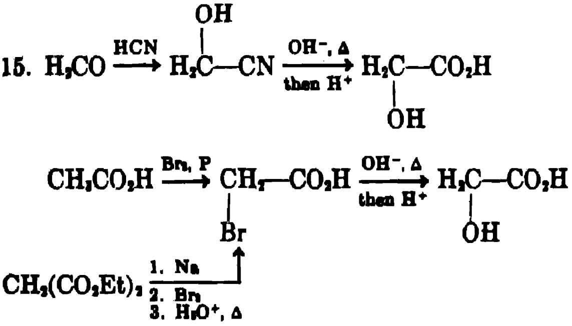
11. Smaller.

12. (a) The acetoacetate has sufficient enol character to give a positive test with aq. $FeCl_3$, but the malonate does not. (b) The α,α-dimethylacetoacetate cannot enolize, and hence it will not give a color with aq. $FeCl_3$, but the butyroylacetate, $CH_3CH_2CH_2CO—CH_2—CO_2CH_3$, will. (c) Triolein is unsaturated and will decolorize aq. $KMnO_4$ or Br_2/CCl_4 solutions, whereas the saturated tristearin will not.

13. 36 ml.

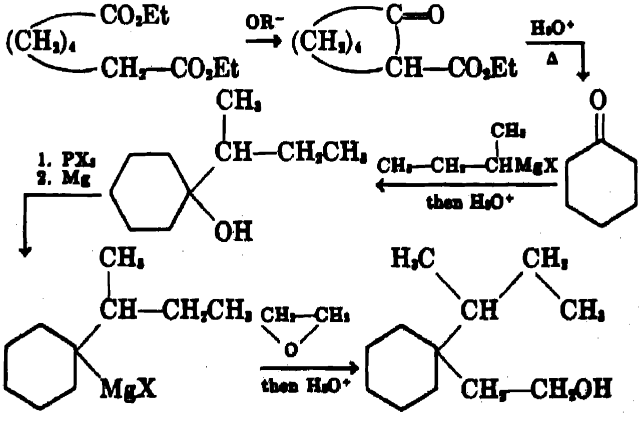
14. 6.16 g.

15.

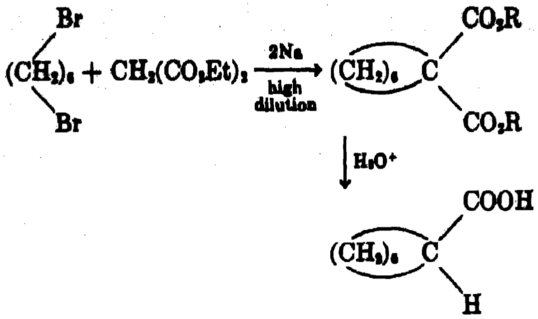


16. *n*- > iso- ≫*t*-butyl alcohols;
n-butyric > isobutyric > trimethylacetic acids.

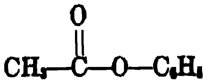
17.



18.

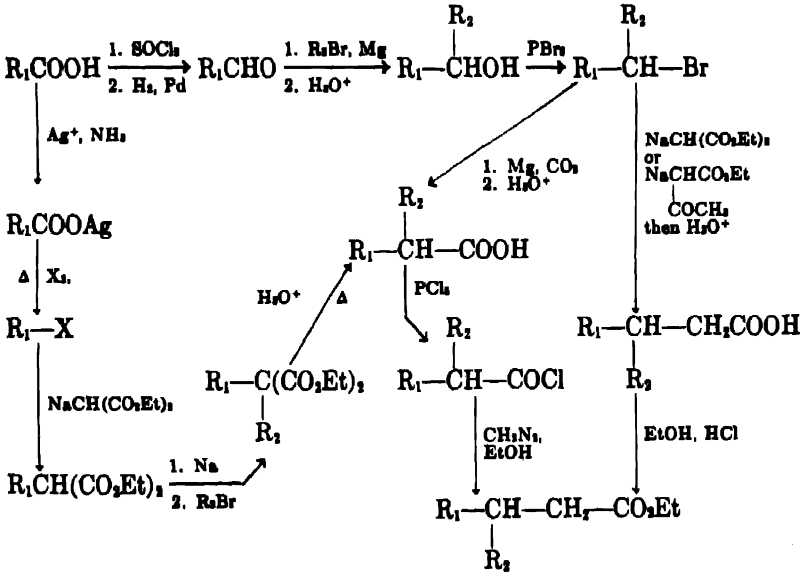


19.



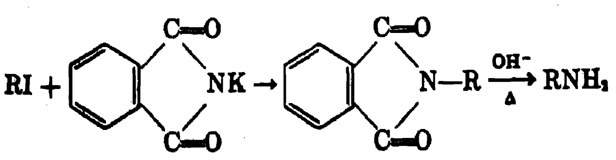
$CH_3-\overset{O}{\overset{\|}{C}}-O-C_6H_5$

20. Let $C_6H_{11} = R_1$ and $C_7H_{13} = R_2$.



Set 16 (page 420)

1. *p*H = 12
2.

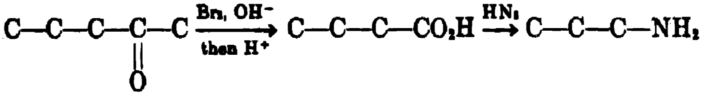


R = *n*—C_3H_7 ∴ 4.8 g RNH_2 for two steps.

3. $RI \xrightarrow{KCN} RCN \xrightarrow{LiAlH_4} R{-}CH_2NH_2$

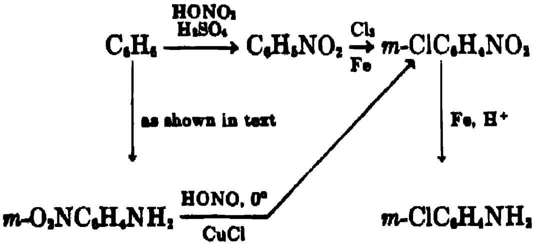
∴ For two steps, get same yield.

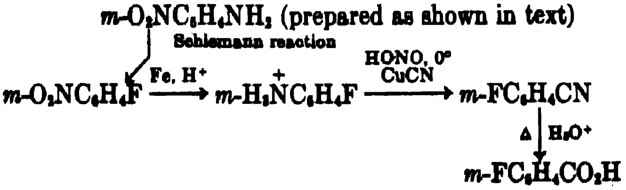
4. 50.3 ml.
5. 88.
6. 1.2%.
7. 0.012 *M*.
8. Dissolve in chloroform, extract the amine with 5% hydrochloric acid, and recover the amine by making the aqueous phase basic. Extract the octanoic acid with 5% NaOH and regenerate the organic acid by acidifying the alkaline solution. Distill off the chloroform to isolate the 2-octanol.

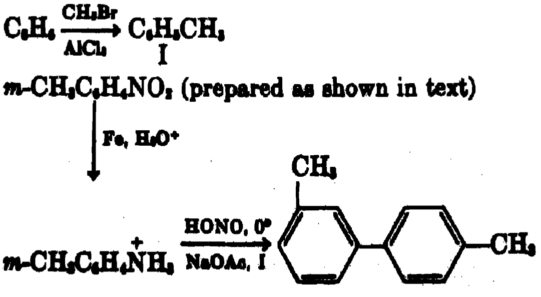
9. 

$$C{-}C{-}C{-}\underset{\underset{O}{\|}}{C}{-}C \xrightarrow[\text{then } H^+]{Br_2,\ OH^-} C{-}C{-}C{-}CO_2H \xrightarrow{HN_3} C{-}C{-}C{-}NH_2$$

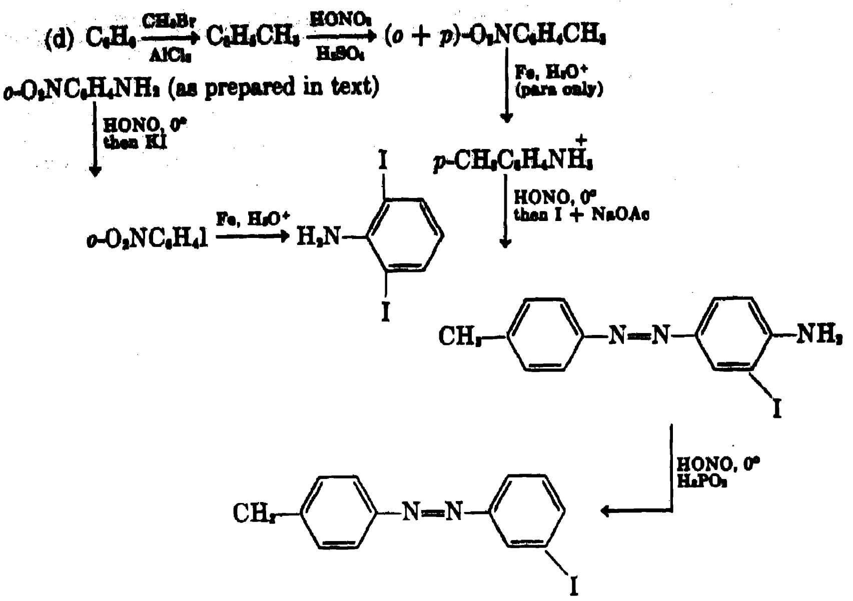
10. Treat with nitrous acid. The primary amine will give off a gas, whereas the secondary amine will give a bluish-green oil; or, treat a sample with $CHCl_3$ plus aq. NaOH. The *n*-pentylamine will produce an unpleasant garlic-like odor.

11. (a) 

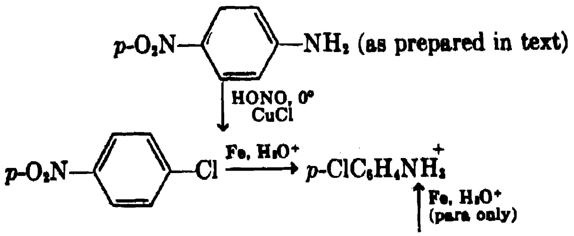
(b) 

(c) 

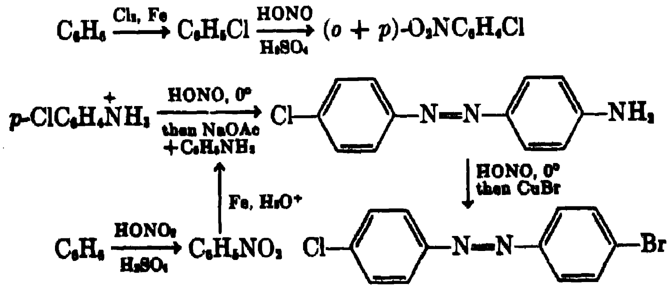
C_6H_6
CH₃Br
AlCl₃
$C_6H_5CH_3$
I
m-$CH_3C_6H_4NO_2$ (prepared as shown in text)
Fe, H₃O⁺
m-$CH_3C_6H_4\overset{+}{N}H_3$
HONO, 0°
NaOAc, I
CH₃
CH₃


(d) $C_6H_6 \xrightarrow[AlCl_3]{CH_3Br} C_6H_5CH_3 \xrightarrow[H_2SO_4]{HONO_2} (o + p)\text{-}O_2NC_6H_4CH_3$
Fe, H_3O^+ (para only)
$p\text{-}CH_3C_6H_4N\overset{+}{H_3}$
HONO, 0° then I + NaOAc
$o\text{-}O_2NC_6H_4NH_2$ (as prepared in text)
HONO, 0° then KI
$o\text{-}O_2NC_6H_4I \xrightarrow{Fe,\ H_3O^+} H_2N\text{-}$
I
I
CH_3
N=N
NH_2
I
HONO, 0° H_3PO_2
CH_3
N=N
I

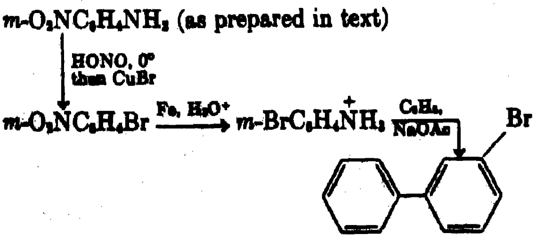
(e) Will couple $p\text{-}XC_6H_4N_2^+$ with $C_6H_5NH_2$, then replace the NH_2 group by the other X atom.


$p\text{-}O_2N$
NH_2 (as prepared in text)
HONO, 0° CuCl
$p\text{-}O_2N$
Cl $\xrightarrow{Fe,\ H_3O^+} p\text{-}ClC_6H_4N\overset{+}{H_3}$
Fe, H_3O^+ (para only)

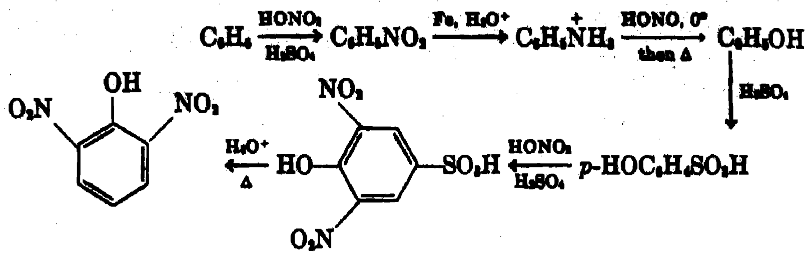
or


$C_6H_6 \xrightarrow{Cl_2,\ Fe} C_6H_5Cl \xrightarrow[H_2SO_4]{HONO} (o + p)\text{-}O_2NC_6H_4Cl$
$p\text{-}ClC_6H_4N\overset{+}{H_3}$
HONO, 0° then NaOAc $+C_6H_5NH_2$
Cl
N=N
NH_2
Fe, H_3O^+
HONO, 0° then CuBr
$C_6H_6 \xrightarrow[H_2SO_4]{HONO_2} C_6H_5NO_2$
Cl
N=N
Br

(f)

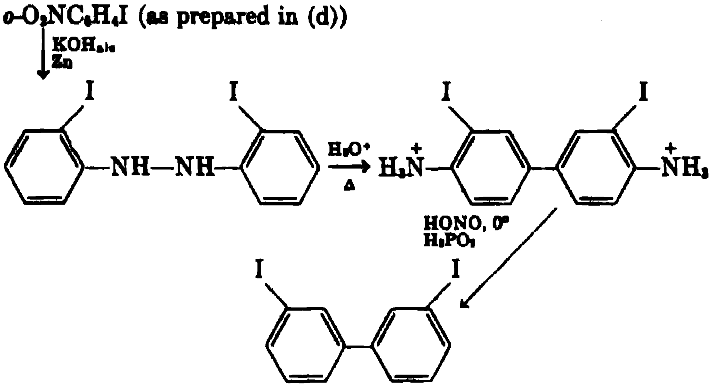

$m\text{-}O_2NC_6H_4NH_2$ (as prepared in text)
HONO, 0° then CuBr
$m\text{-}O_2NC_6H_4Br \xrightarrow{Fe,\ H_3O^+} m\text{-}BrC_6H_4N\overset{+}{H_3}$
C_6H_6, NaOAc
Br

(g)



$C_6H_6 \xrightarrow[H_2SO_4]{HONO_2} C_6H_5NO_2 \xrightarrow{Fe,\ H_3O^+} C_6H_5\overset{+}{N}H_3 \xrightarrow[\text{then } \Delta]{HONO,\ 0°} C_6H_5OH$
H_2SO_4
$p\text{-}HOC_6H_4SO_3H$
$HONO_2$
H_2SO_4
SO_3H
HO
NO_2
O_2N
H_3O^+
Δ
OH

(h)



(i) $o\text{-}O_2NC_6H_4NH_2$ (as prepared in text)

$\downarrow$ 1. HONO, 0° 2. BF_4^-

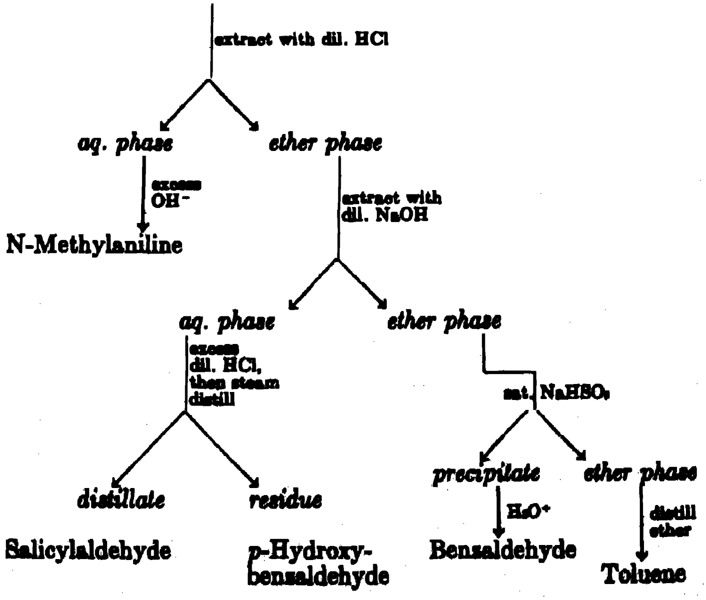
$o\text{-}O_2NC_6H_4N_2BF_4 \xrightarrow[NaNO_2]{Cu} o\text{-}C_6H_4(NO_2)_2$

(j) $C_6H_5NH_2$ (as prepared in (e))

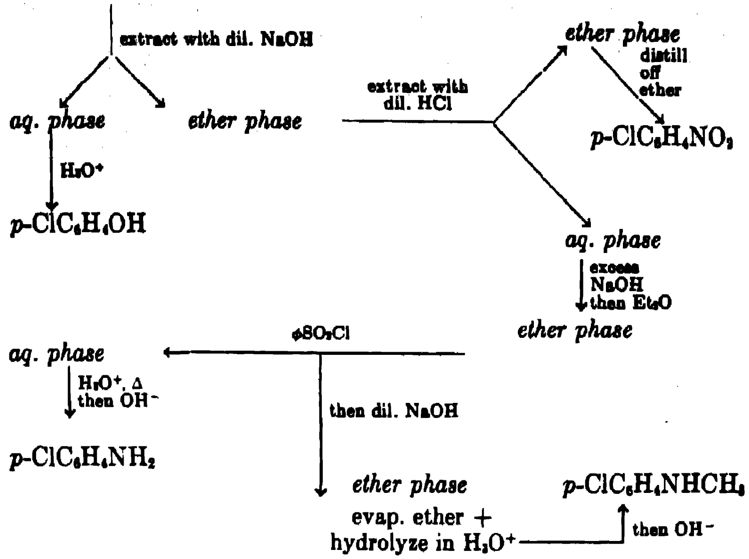
$\downarrow 3Br_2$

$2,4,6\text{-}Br_3C_6H_2NH_2 \xrightarrow[\text{then } H_3PO_2]{HONO,\ 0°} 1,3,5\text{-}Br_3C_6H_3$

12. (a) Dissolve mixture in ether

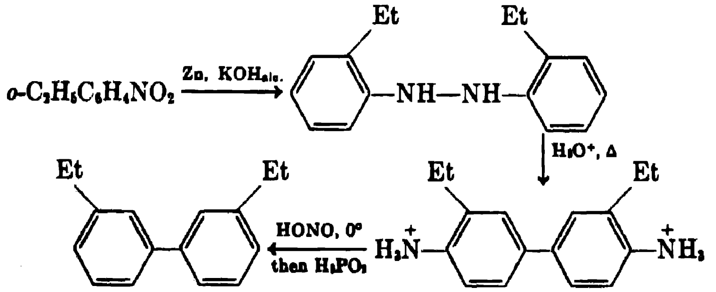


(b) Dissolve mixture in ether



13. (a) $C_6H_5NH_3Cl$ dissolves in H_2O, and also would give a precipitate with Ag^+; $ClC_6H_4NH_2$ will do neither. (b) Treat sample with HONO at 0–5 and pour a few drops into alk. naphthol; only $CH_3C_6H_4NH_2$ would give red color or precipitate.

14.



15. Presence of the ions indicates that it ionizes, and neutrality shows that both ions, Cl^- and ϕN_2^+, are ions of a strong acid and base, respectively. Hence, ϕN_2OH is a strong base, i.e., completely ionized in solution.

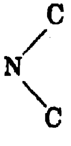
16. 82 g.

17. cyclohexylamine > N-methylaniline > aniline > p-nitroaniline.

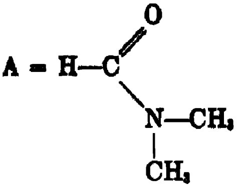
18. The more electron-withdrawing are the substituents in the benzenediazonium nucleus, the more electrophilic is the ion and the more vigorously does it attack another aromatic ring. Hence, toluenediazonium ion would be a still more weakly coupling agent than benzenediazonium ion.

Set 17 (page 438)

1. (a) Therefore three carbons to work with.
   (b) Therefore probably an amide, imide, or nitrile.
   (c) Therefore amine is secondary, i.e.,



(d) Hence the acid is formic. Therefore,



2. 100 ml.

3. N,N-Dimethylacetamide > N-methylacetamide > acetamide > acetic acid. Amides have a greater polar character than acids, and the N-alkyl amides have a larger molecular weight.

4. (a) The amide is water soluble.
   (b) The ammonium acetate ionizes upon dissolving and would give off ammonia immediately when cold OH^- is added.
   (c) Use the nitrous acid test given in the text to distinguish primary from secondary nitroalkanes.
   (d) Hydrolyze and test product for formic acid with Tollens' reagent. The isocyanide will give a positive test.
   (e) Ethyl nitrite will hydrolyze in water and yield soluble products; nitroethane is inert to H_2O.

5. Nitromethane is a very polar molecule and therefore is insoluble in nonpolar liquids such as hydrocarbons.

6. The ratio of polar (OH) to nonpolar (hydrocarbon) fragments in methanol is larger than in propanol, thereby making methanol the more polar liquid. It will therefore be the better solvent for the CH_3NH_3Cl salt.

7. First write down the deductions which can be made from each experimental observation:

A = $C_5H_{10}O_4$—∴ there are five C's to work with;

A + Na → H_2—∴ at least one active H.

Neg. 1,2-glycol—∴ no two OH's on adjacent C's.

Pos. iodoform test—∴ CH_3—CHOH— or CH_3—CO— structure present.

No 2,4-DNPH—∴ no ketone or aldehyde; hence have CH_3—CHOH— and not CH_3—CO—.

$C_5H_{10}O_4 + Ac_2O \rightarrow C_9H_{14}O_6$—since the gain is $2(C_2H_2O)$, have 2 OH's.

Hydrolysis → C + D—∴ A cannot be an amide because there is no nitrogen; nor can A be an ether, since ethers do not hydrolyze in dil. acid; so we suspect A is an ester. Hence, C and D are alcohol and acid.

C neutral—∴ suspect it to be the alcohol.

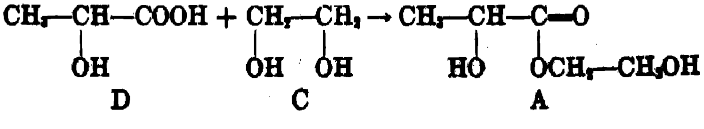
C gives pos. 1,2-glycol test, so must contain two adjacent OH's. One OH arose from the hydrolysis.

D acidic—∴ suspect D is the acid.

D changes color of Ce^{+4}—∴ believe it has an OH on side chain.

D gives pos. iodoform and neg. 2,4-DNPH—∴ must have CH_3—CHOH— structure. Since D must have COOH and CH_3—CHOH— structures, this accounts for 3 C's in A.

C has at least 2 C's of A (since it has 1,2-glycol group)—∴ all carbons in A are accounted for. Putting C and D together, one gets



$$\underset{\textbf{D}}{CH_3\text{—}\underset{OH}{\underset{|}{CH}}\text{—}COOH} + \underset{\textbf{C}}{\underset{OH}{\underset{|}{CH_2}}\text{—}\underset{OH}{\underset{|}{CH_2}}} \rightarrow \underset{\textbf{A}}{CH_3\text{—}\underset{HO}{\underset{|}{CH}}\text{—}\underset{OCH_2\text{—}CH_2OH}{\underset{|}{C}}{=}O}$$

Checking back, the structure for A would agree with the properties given in the problem.

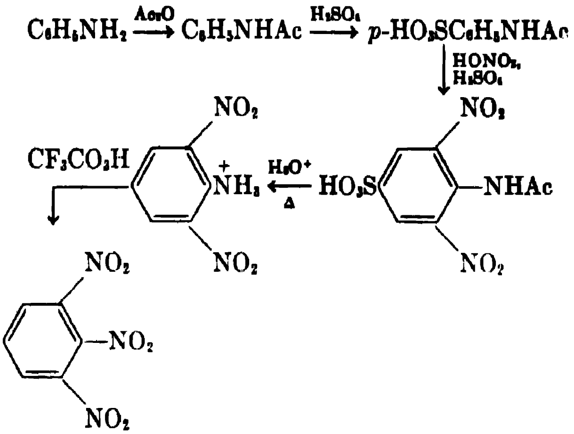
8. Treat the amido ester with cold nitrous acid which will replace the NH_2 by OH without appreciable hydrolysis of the ester group occurring.

9. No, because both compounds would distill with the steam in proportion to their vapor pressures near 100°.

10. 168 g.

11. Yes, the nitro acids would dissolve in the aqueous alkali and at least the oxidizing agent would be a homogeneous mixture.

12.



13. (a) $(CH_3)_2CH—(CH_2)_2—CH_2OH \rightarrow (CH_3)_2CH—(CH_2)_3—CH_2NO_2$

It can be seen that an alcohol is to be converted into a nitroalkane containing one more CH_2 group. So, plan backwards and recall that nitroalkanes are prepared from alkyl halides; that alkyl halides may be prepared from alcohols; that alcohols may be prepared by reduction of carboxylic acids or aldehydes; that of the chain-lengthening methods, either the aldehyde, acid, or alcohol may be obtained from the Grignard, and that the Grignard is made from the alkyl halide, which may be prepared from the given alcohol. This can be expressed by equations, where R = $(CH_3)_2CH—(CH_2)_2—$

$$ROH \xrightarrow{PBr_3} RBr \xrightarrow{Mg} RMgBr \xrightarrow[2.\ H_3O^+]{1.\ H_2CO} RCH_2OH \xrightarrow{KBr,\ H_2SO_4} RCH_2Br \xrightarrow{KNO_2} RCH_2NO_2$$

Of course, several other routes are possible, for example:

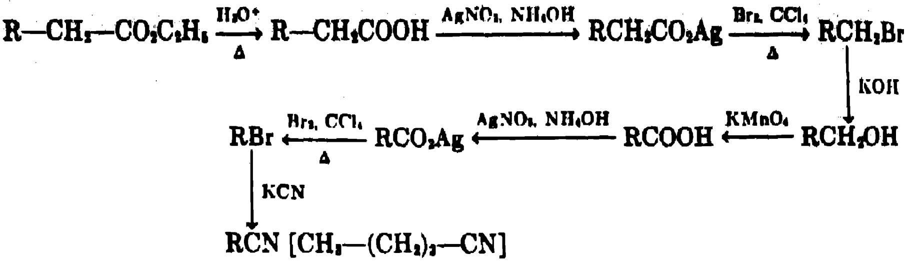
$$ROH \xrightarrow{PBr_3} RBr \xrightarrow{KCN} RCN \xrightarrow{LiAlH_4} RCH_2NH_2 \xrightarrow[2.\ PX_5]{1.\ C_6H_5COCl} RCH_2X \xrightarrow{KNO_2} RCH_2NO_2$$

Or

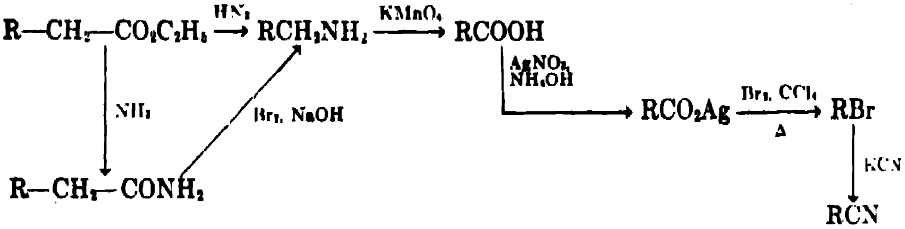
$$\begin{tikzcd}
ROH \arrow[r, "SOBr_2"] & RBr \arrow[r, "Mg"] & RMgBr \arrow[r, "1.\ CO_2", "2.\ H_3O^+"'] \arrow[d, "1.\ HC(OEt)_3", "2.\ H_3O^+"'] & R—COOH \arrow[r, "R'OH,\ H_2SO_4"] & R—COOR' \arrow[r, "NH_3"] & RCONH_2 \arrow[d, "LiAlH_4"] \\
 & & R—CHO \arrow[r, "LiAlH_4"] & R—CH_2OH \arrow[d, "HX,\ ZnCl_2"] & & RCH_2NH_2 \arrow[ll, "HONO"'] \\
 & & RCH_2NO_2 & R—CH_2X \arrow[l, "KNO_2"'] & &
\end{tikzcd}$$

(b) $CH_3-(CH_2)_4CO-OC_2H_5 \rightarrow CH_3-(CH_2)_3-CN$

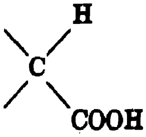
Here, a CH_2 group is to be cut off. Of the ways to make a nitrile, one is from the alkyl halide and one from the amide. Among the degradation methods, one changes an acid to an alkyl halide. Thus, a route is suggested, where R = $CH_3-(CH_2)_3-$

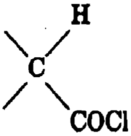


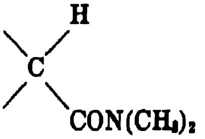
Other routes come to mind, for example:

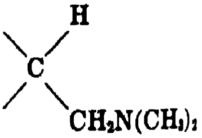


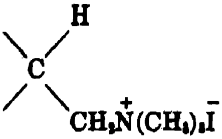
14.

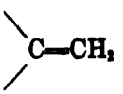

I

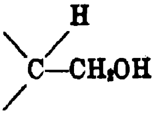

II


III

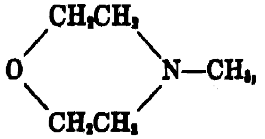
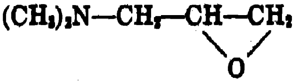

IV


V


VI


VII

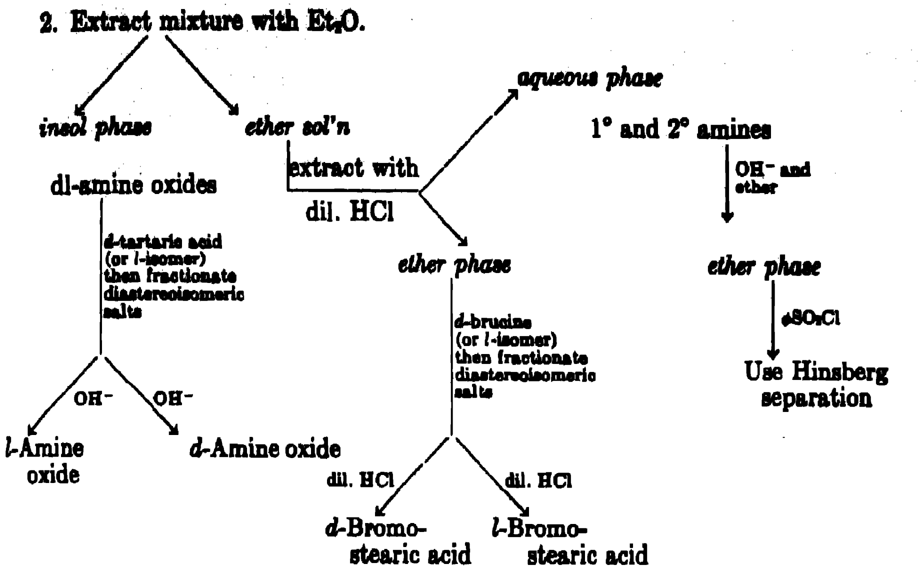
15. (a) $(C_2H_5)_2C{=}NOH$; (b) $C_3H_7-CON(CH_3)_2$; (c) $C_4H_9-CONH_2$;

(d)  

Set 18 (page 457)

1. Four

2.



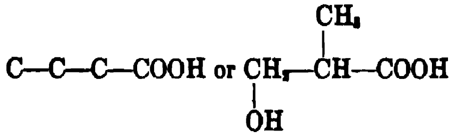
3. (a) Gives 2,4-DNP; therefore, $>C{=}O$ is present.

Ce^{+4} is red color; therefore, ROH. (No ϕOH, since only four C's.)

(b) $C_4H_8O_2 \xrightarrow{AcCl} C_6H_{10}O_3$; therefore, one OH

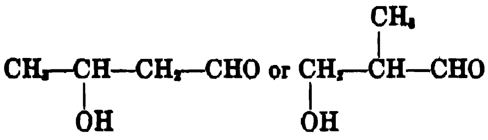
(c) $A \xrightarrow{\text{oxid.}} RCOOH$; therefore, oxidizing CH_2OH or CHO

(d) Therefore, B =



$$C-C-C-COOH \text{ or } \underset{\displaystyle OH}{CH_2}-\overset{\displaystyle CH_3}{CH}-COOH$$

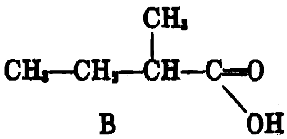
Therefore, A =



$$CH_3-\underset{\displaystyle OH}{CH}-CH_2-CHO \text{ or } \underset{\displaystyle OH}{CH_2}-\overset{\displaystyle CH_3}{CH}-CHO$$

4. $A \xrightarrow[\Delta]{H_2O} B + C$

B = H_2O, insol., alkali sol.; therefore, acid RCOOH is the only structure for $C_5H_{10}O_2$ to give asymmetric carbon:



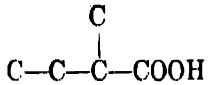
$$CH_3-CH_2-\overset{\displaystyle CH_3}{CH}-C(=O)OH$$

B

C is water soluble; therefore, CH_3CH_2OH.
Therefore, A = $CH_3-CH_2-CH(CH_3)-CO_2C_2H_5$.

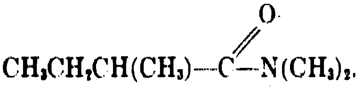
5. Elemental analysis and molecular weight determination would indicate the same molecular formula; hence, isomers. Hydrogenation would yield butyric acid in both cases, showing that they are merely *cis-trans* isomers. The infrared spectra would differ essentially only in the C=C region, exhibiting bands characteristic for *cis* in one case and for *trans* in the other.

6. (a) Hence, amide or imide. (b) Amine is secondary; therefore, at least two C's are attached to N. Therefore, acid can have maximum of five C's, and only one structure with C, H, and O solely meets this condition:



$$C—C—C(C)—COOH$$

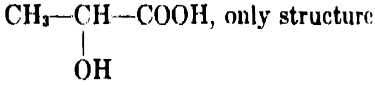
Therefore, $C_7H_{15}NO$ =



$CH_3CH_2CH(CH_3)—C(=O)—N(CH_3)_2$.

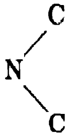
7. (a) No plane of symmetry.

(b) A = amide or imide. Also, part of A is



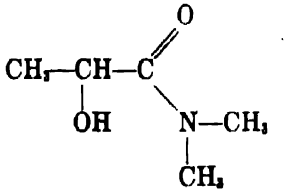
$CH_3—CH(OH)—COOH$, only structure possible for asymmetric $C_3H_6O_3$ (optically active).

(c) Therefore, amine is secondary:



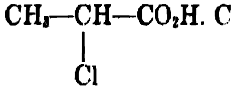
$C—N—C$

Therefore, A =



$CH_3—CH(OH)—C(=O)—N(CH_3)—CH_3$

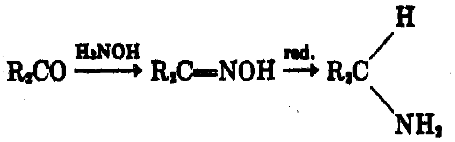
8. Since A is recovered from alkali unchanged, it is an acid, not an acid halide; hence, A =



$CH_3—CH(Cl)—CO_2H$. Cl must be on α C for A to be optically active.

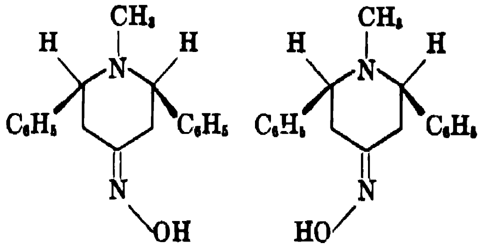
9. (a) Case 3, $n = 5$; active = 4, meso = 4, $r = 2$
   (b) Case 2, $n = 6$; active = 32, meso = 4, $r = 16$
   (c) Case 1, $n = 4$; active = 8, meso = 0, $r = 4$

10. Physical properties in general depend upon *intra-* and *inter*molecular forces. The intramolecular forces are certainly not the same in geometric isomers and often the difference in shapes will produce different intermolecular forces, e.g., pack differently in the solid state; hence, geometric isomers have different physical properties. Optical isomers have identical interatomic distances within the molecules. Hence, they have identical intramolecular forces as well as intermolecular forces. Hence, they have identical physical properties except toward asymmetric environments.

11. 
$$R_2CO \xrightarrow{H_2NOH} R_2C{=}NOH \xrightarrow{red.} R_2C\begin{smallmatrix}H\\NH_2\end{smallmatrix}$$

$R_1 = CH_3$, $R_2 = CH_3CH_2CH_2$—
$R_1 = CH_3$, $R_2 = (CH_3)_2CH$—
$R_1 \neq R_2$ or have no asymmetric carbon

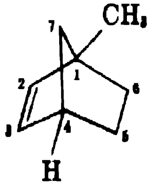
12. Compound I optically inactive, has plane of symmetry. Oxime optically active and resolved.



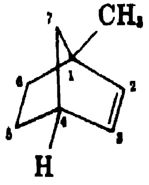
Nonsuperposable mirror images

13. (R)-3-Methylcyclopentene.

14.



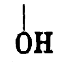
1(R),4(S)



1(S),4(R)

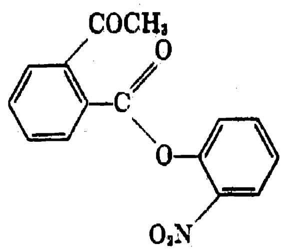
15. No.

Set 19 (page 509)

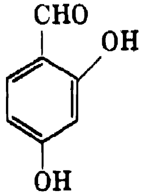
1. (a) *1* = amide or cyclic imide.
   (b) Therefore, alcohol of four carbon atoms, has asymmetric carbon. Only one such alcohol =  $$C{-}C{-}\underset{\displaystyle OH}{\underset{|}{C}}{-}C.$$
   (c) Iodoform test only confirmatory. Therefore, *1* = $$CH_3{-}CH_2{-}\underset{\displaystyle CH_3}{\underset{|}{CH}}{-}CONH_2$$

2. Carbonyl; ketone; aromatic; acyl group. *2* possibly an ester; could be an amide. *4* = phenol and NO_2 group, steam distillable, hence *o*-nitrophenol. *3* : still ketone; methyl ketone; acid. Therefore, *o*, *m*, or *p*-acetylbenzoic acid. Oxid. → phthalic acid; therefore, *3* = *o*-$CH_3COC_6H_4COOH$.

2 =

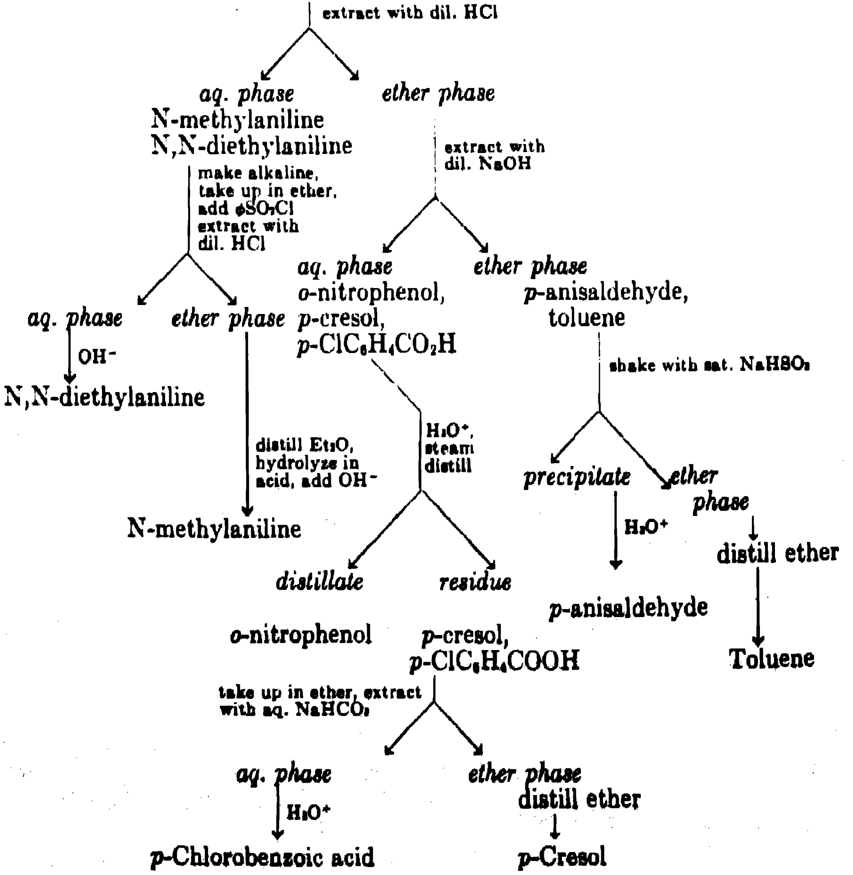


3. 5 = aldehyde; phenol or enol; two OH groups:

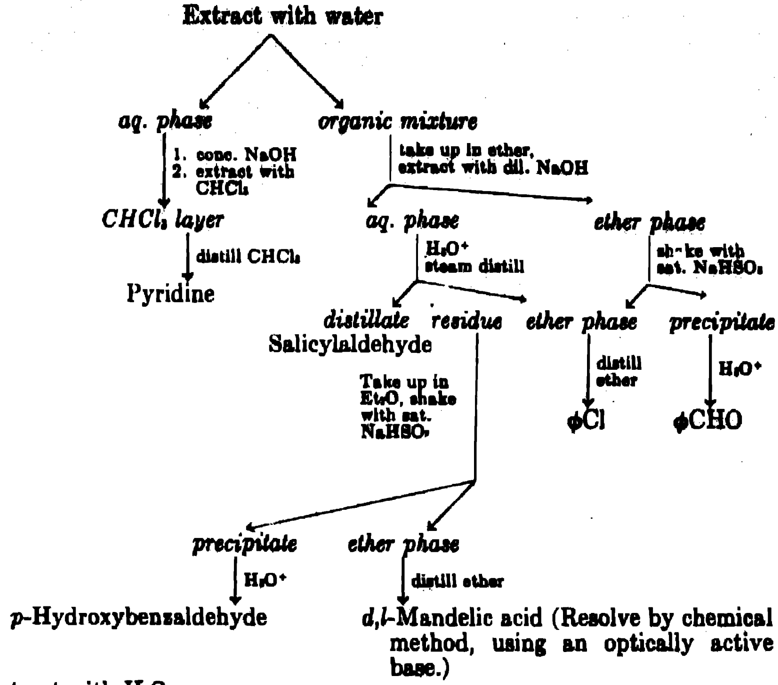


Need more information about positions of second OH group. One is probably ortho to CHO to give deep color in FeCl$_3$ test.

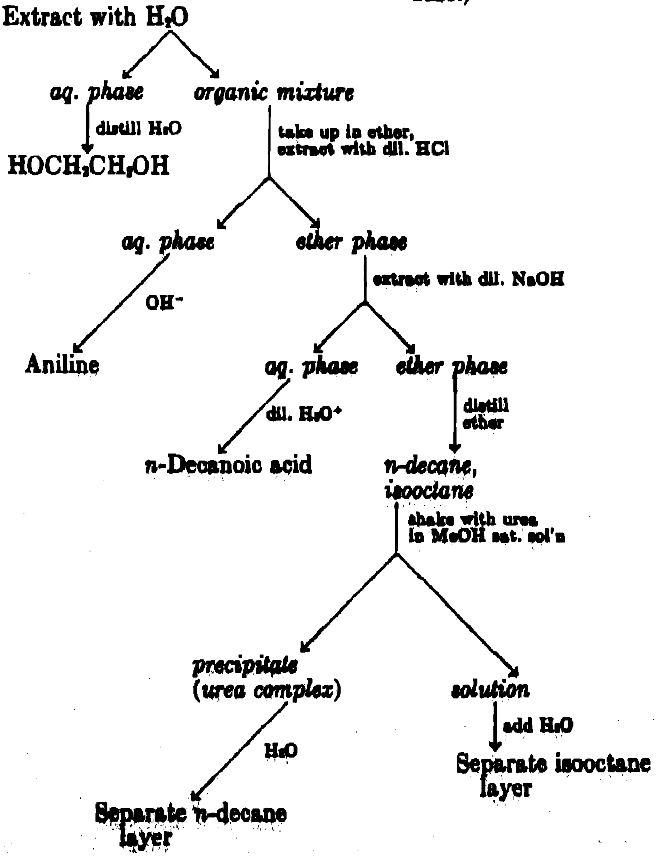
4. (a) Dissolve in ether



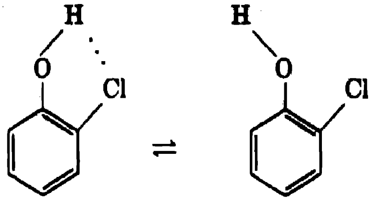
(b)


Extract with water
aq. phase
1. conc. NaOH
2. extract with CHCl₃
CHCl₃ layer
distill CHCl₃
Pyridine
organic mixture
take up in ether, extract with dil. NaOH
aq. phase
H₃O⁺
steam distill
distillate
Salicylaldehyde
residue
Take up in Et₂O, shake with sat. NaHSO₃
precipitate
H₃O⁺
p-Hydroxybenzaldehyde
ether phase
distill ether
d,l-Mandelic acid (Resolve by chemical method, using an optically active base.)
ether phase
shake with sat. NaHSO₃
ether phase
distill ether
φCl
precipitate
H₃O⁺
φCHO

(c)


Extract with H₂O
aq. phase
distill H₂O
HOCH₂CH₂OH
organic mixture
take up in ether, extract with dil. HCl
aq. phase
OH⁻
Aniline
ether phase
extract with dil. NaOH
aq. phase
dil. H₃O⁺
n-Decanoic acid
ether phase
distill ether
n-decane, isooctane
shake with urea in MeOH sat. sol'n
precipitate (urea complex)
H₂O
Separate n-decane layer
solution
add H₂O
Separate isooctane layer

5. Since the OH is *o*- and *p*-directing, expect the two products to be *o*- and *p*-chlorophenol. *o*-Chlorophenol can exist as two isomers through intramolecular hydrogen bonding, and it gives rise to two OH bands. Irrespective of which way the O—H points in *p*-chlorophenol, there results only one isomer; hence, only one band. Therefore A is the ortho isomer and B is the para isomer.

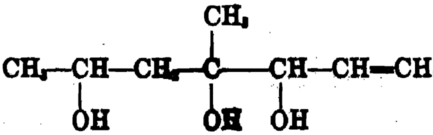


6. $\nu_{C=O} \sim 1725\ cm^{-1}$ $\nu_{C-O-C} \sim 1178\ cm^{-1}$ no ν_{OH} *cis* $\nu_{C=C}$ 700 *or* *trans* $\nu_{C=C}$ 967 cm^{-1}	$\nu_{C=O}$ 1680 cm^{-1} ν_{O-H} 3640	$\nu_{C=O} \sim 1750\ cm^{-1}$ $\nu_{C-O-C} \sim 1178\ cm^{-1}$ vinyl $\nu_{C=C} \sim 910\ cm^{-1}$ no ν_{OH}
6	*7*	*8*

7. λ_m = 229 mμ for α,β-enone. ν at 1665, 1640 cm^{-1} for C=C—C=O.
ν = 3640 cm^{-1} for single OH, ∴ sterically hindered OH.
ν = 1070 cm^{-1} for alkyl ether.

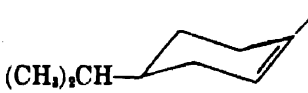
8. First write down the deductions which can be made from each experimental observation:

10 $\xrightarrow{Na}$ H_2. ∴ *10* has an active H, perhaps an alcohol, acid; or 1-alkyne (≡C—H).
10 insol. alkali, ∴ not an acid.
10 decolorizes MnO_4^-, ∴ unsaturated and with active H.
10 $\xrightarrow{Pb(OAc)_4}$ *11* + *12*. Note that *11* and *12* together have the same number of O's and two less H's, so *10* is probably a 1,2-glycol.
12 $\xrightarrow{Tollens'}$ Ag, ∴ *12* is an aldehyde.
12 decolorizes MnO_4^-, ∴ unsaturated. This gives us C=C—CHO, and to comply with the molecular formula, merely the correct number of H's need be added. *12* then, is CH_2=CH—CHO.
11 does not reduce Tollens', ∴ not an aldehyde. *11* forms bisulfite addition compound; since it is not an aldehyde, *11* must be a methyl ketone.
11 gives pos. iodoform test, ∴ has $COCH_3$.
11 $\xrightarrow{Na}$ H_2, ∴ has active H. Not enough O's for an acid; hence, may be OH. This gives for *11*: CH_3—CO—CH_2—CHOH—CH_3 or CH_3—CO—CHOH—C_2H_5.
11 $\xrightarrow[\Delta]{Cu}$ *13*, losing two H's, hence have dehydrogenation. Thus, *13* is a diketone. Has properties of an enol; thus is 1,3-diketone, CH_3—CO—CH_2—CO—CH_3. ∴ *11* is CH_3—CO—CH_2—CHOH—CH_3 and *10* has structure

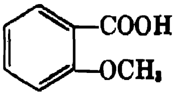


$$CH_3-\underset{OH}{CH}-CH_2-\underset{OH}{\overset{CH_3}{C}}-\underset{OH}{CH}-CH=CH_2$$

9. *14* is oxidized to the 1,2-diketone, but a fraction of the product enolizes and the two tautomers are isolated. Thus, *15* is the yellow diketone, has the IR band at 1715 cm^{-1}. *16* is the enol, gives a FeCl$_3$ test, has IR bands for hydrogen bonded OH and C=O groups and a C=C band (1630 cm^{-1}).

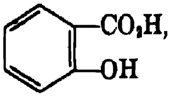
10. 

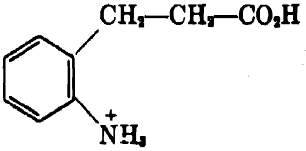
$\lambda_m \sim 330$ mμ; $\nu_{C=O} \sim 1680$ cm^{-1}

11. 

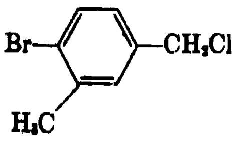
12. ~1776 cm^{-1}.

13. (a) $CH_3CH_2COCH_2CO_2C_2H_5$ enolic and soluble in aq. alkali, the other keto ester is not. (b) The first compound is an amine and soluble in dilute hydrochloric acid, the other compound is an amide and insoluble in the acid. (c) The first compound is an aliphatic primary amine and soluble in dil. aq. HCl, the other compound is a secondary aromatic amine and insoluble in the acid. (d) Glycerol is soluble in water, insoluble in ether. The glycerol triethyl ether has just the reverse solubility properties. (e) Pthalimide is soluble in conc. aq. KOH, the other compound is not. (f) Sodium benzoate is soluble in water, the acid is not. (g) Sodium benzenesulfonate is soluble in dil. aq. sulfuric acid, the sodium benzoate would precipitate benzoic acid.

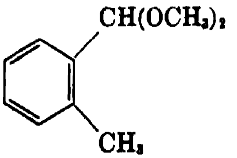
14. (a) C_6H_5COOH, $H_3\overset{+}{N}-CH_2COOH$, and $\overset{+}{N}H_4$ ion. (b) $CH_3-(CH_2)_3-\overset{+}{N}H_3$, CO_2, $\overset{+}{N}H_4$, and $HO_2C-(CH_2)_3-CH_3$. (c) $(C_2H_5)_2CO$ and $H_3\overset{+}{N}-NH-C_6H_5$. (d) 

$HOCH_2CH_2\overset{+}{N}H(C_2H_5)_2$, and HO_2C-CH_3. (e) 

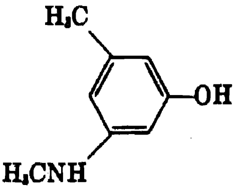
15. (a) Benzyl bromide would give a white precipitate with aq. AgNO$_3$ at room temperature, the other would not; (b) Propylene glycol would give a positive 1,2-glycol test with periodic acid and AgNO$_{3\,aq.}$; (c) Isopropyl alcohol is a secondary alcohol and would give a positive Lucas test in less than 5 min; (d) The 1,1 isomer is an acetal and would hydrolyze in dilute acid and then give a 2,4-dinitrophenylhydrazone, the 1,2 isomer would not; (e) Phenylacetaldehyde is an aliphatic aldehyde and would give a positive test with Benedict's reagent.

16. 

Compound *17*

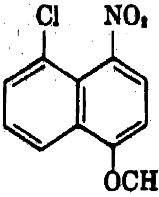
17. 

Compound *21*

18. 

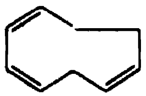
Compound *23*

19.



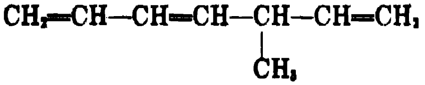
Compound *24*

20. IR shows conjugated and isolated C═C bonds, all *cis*. UV shows only two C═C bonds to be conjugated, not three. The n.m.r. shows two allyl CH_2 methylenes, one bisallyl methylene, and six vinyl protons.



28

21.



$$CH_2{=}CH{-}CH{=}CH{-}\underset{\displaystyle CH_3}{\underset{|}{CH}}{-}CH{=}CH_2$$

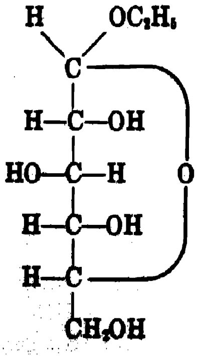
22. *29* in bottle 1; *30* in bottle 3; *31* in bottle 2.

Set 20 (page 530)

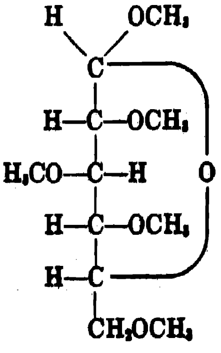
1. Ten
2. The amino acids are polar; hence, a polar solvent is needed. Hexane is nonpolar.
3. (a) Mol. wt. = 273; (b) 40 ml; (c) 23.3 ml.
4. Anion.

Set 21 (page 558)

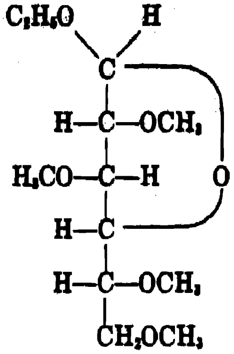
1. (a) Active = 32, meso = 0; (b) active = 8, meso = 2; (c) active = 56, meso = 8.
2. Four.
3. 1.58 g.
4. (a)



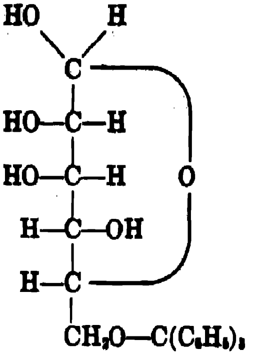
(b)



(c)

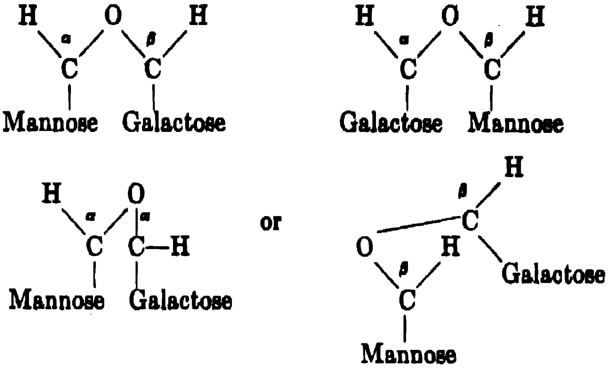


(d)



5. 32.4 g.

6.



That is, either sugar unit can have an α or β anomeric structure.

7. 32.5°.

8. 66° from the sugar, 62.7° from the glucosides.

9. 25°.

10. The aldehyde content is so small that Schiffs reagent cannot detect this small a quantity but Tollens' and Fehling's reagents are sensitive enough to give positive tests.

11. Because the carbonyl carbon is already in the form of a stable hemiacetal and only one alcohol molecule will react.

12. 32.6%.

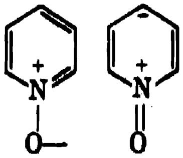
Set 22 (page 571)

1. Pyridine, like dioxane, dissolves in water because of hydrogen bonding of water with the hetero atoms and absence of any steric hindrance by groups near the hetero atoms. The hydrogen bonding between water and benzene or thiophene is too weak to bring about any appreciable solubility of these two compounds in water.

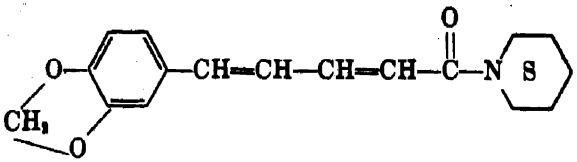
2. $K_b \sim 10^{-10}$

3. 3.

4. 4.

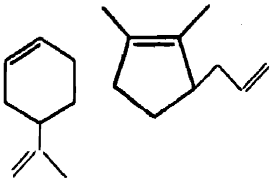


5.



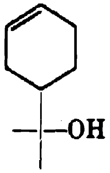
Set 23 (page 581)

1. (a) one; (b)

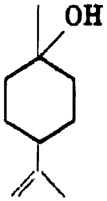


Most likely

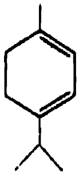
(c)



or



2. (a)

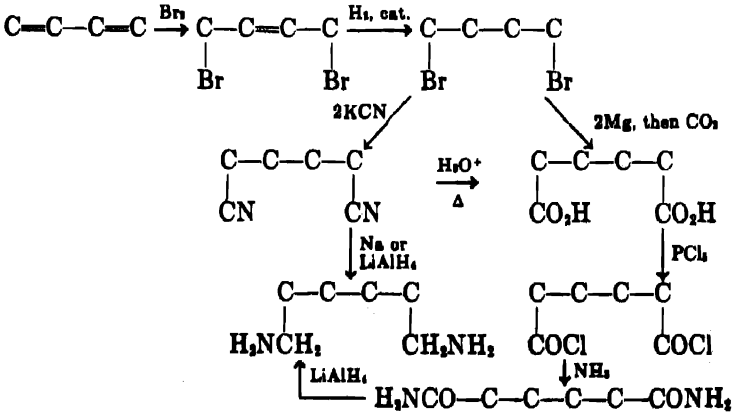


(b) In the aq. oxidation, the hydrocarbon probably adds two H_2O molecules to give the di-tertiary alcohol preceding oxidative cleavage.

Set 24 (page 592)

1. Both are polyamides.

2.



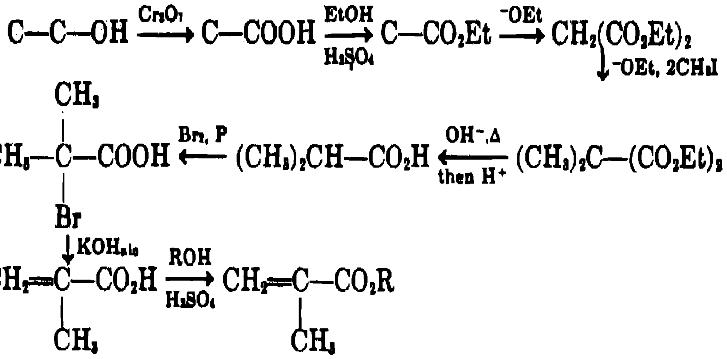
3. 278 ml.

4. 25 ml.

5. (a) Cotton would give the Molisch test, nylon would not. Supposedly, nylon would give the Biuret test, cotton would not. Nylon, boiled in acid, would release ammonia, cotton would not. Cotton boiled in dil. acid, cooled, and neutralized, would reduce Tollens' or Fehling's solutions, nylon would not.

(b) Rayon would dissolve in cold conc. NaOH, rayon acetate would not; rayon acetate would dissolve in organic solvents like acetone, ethyl acetate, or methylene chloride, rayon would not.

6.



$$\text{C—C—OH} \xrightarrow{Cr_2O_7} \text{C—COOH} \xrightarrow[H_2SO_4]{EtOH} \text{C—}CO_2Et \xrightarrow{^-OEt} CH_2(CO_2Et)_2 \xrightarrow{^-OEt,\ 2CH_3I} (CH_3)_2C\text{—}(CO_2Et)_2$$

$$(CH_3)_2C\text{—}(CO_2Et)_2 \xrightarrow[\text{then } H^+]{OH^-, \Delta} (CH_3)_2CH\text{—}CO_2H \xrightarrow{Br_2,\ P} CH_3\text{—}\overset{\displaystyle CH_3}{\underset{\displaystyle Br}{C}}\text{—COOH}$$

$$CH_3\text{—}\overset{\displaystyle CH_3}{\underset{\displaystyle Br}{C}}\text{—COOH} \xrightarrow{KOH_{alc}} CH_2{=}\underset{\displaystyle CH_3}{C}\text{—}CO_2H \xrightarrow[H_2SO_4]{ROH} CH_2{=}\underset{\displaystyle CH_3}{C}\text{—}CO_2R$$

APPENDIX[1]

The Solution of Mathematical Problems on Elementary Organic Chemistry

A-1 HOW TO SOLVE PROBLEMS

Every problem, whether it is to figure out how to get to work when the car will not start in the morning, or to determine how many eggs at 60 cents a dozen can be bought for 3 dollars, or to calculate the weight of potassium permanganate that would be required to oxidize a given quantity of ethyl alcohol to acetic acid, is solved essentially in the same manner. One considers the answer, decides what specific fact will give the answer, figures out what is needed to get this fact, and in this fashion works his way back to the original problematic situation. This sets the shortest route from the problem or given data to the answer sought; for obviously, many quantities may be calculated from the given facts, but only a few of these will lead back to the answer. For illustration, the egg problem above is fairly simple. One quickly notes that at 60 cents per dozen, each egg costs 5 cents and, therefore, 3 dollars, or 300 cents, will buy 300/5 = 60 eggs. Or, with equal rapidity, one may have noted that 3 dollars, or 300 cents, divided by 60 cents yields 5; hence, 5 dozen = 60 eggs can be purchased. But, unconsciously what was done? In the first procedure, it was noted mentally that if one knew the price of one egg, then one could get the answer by dividing 300 cents by the price of each egg. In the second route, it was recognized that if one knew how many "60-cents's" there are in 3 dollars, he would know how many dozen eggs could be purchased. This example is easy for two reasons. First, one is very familiar with the units involved (dollars, cents, dozen); and second, the route from the answer back to the given data is short and easily picked out.

For chemical problems, however, special effort must be made to keep in mind the relationships between units, and usually one or more chemical principles or laws must be employed to pass through the successive steps from the answer back to the given information. For example, to calculate the volume at standard conditions of 5.6 g. of nitrogen gas, one uses two chemical principles to get from units of volume in the answer to the given data. First, one uses the relationship between weight, molecular weight, and number of moles, and then he uses Avogadro's law (that 1 mole of any gas occupies 22.4 liters at standard conditions). The route is charted now. Since the molecular weight of nitrogen is 28, and

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[1] This appendix is a revision of a publication which appeared in 1951 in lithograph form in collaboration with Mrs. Gladys Pinkney Labat.

$$\frac{\text{Weight}}{\text{Molecular weight}} = \text{number of moles}$$

then

$$\frac{5.6}{28} = 0.2 \text{ mole}$$

Hence, the volume is 0.2 × 22.4 = 4.48 liters (1).

Herein lies the benefit of solving problems. It provides exercise in the utilization of chemical concepts and principles. These chemical principles can be learned and understood, but, without drill in recalling them when needed, one does not learn to recognize or become familiar with their application. It is the same for a carpenter or machinist who may learn what his tools look like and the name and purpose of each, but it takes actual performance to learn the specific use and advantage of each tool. In solving problems, one becomes more adept in using the chemical principles involved which increases his alertness to their specific applications. It develops thought patterns within the student so that he acquires a subconscious logical approach to solving chemical problems, mathematical and nonmathematical. The more problems one solves, the more natural becomes the process of problem solving, i.e., how to chart a route back from the answer to the given information and invoke the necessary chemical principles. Since all problems, mathematical or otherwise, are handled in the same fashion, the training received in analytical thinking from solving problems is extremely beneficial. Repetition makes many of the thoughts initially requiring concentration become spontaneous or mentally reflexive. When confronted with a situation, if the situation is familiar, one reacts immediately without conscious effort. It is well known, for example, that the more often a mouse travels through a maze, the shorter the time he takes to find his way out.

A-2 COMPOSITION ANALYSES, FORMULAS, AND MOLECULAR WEIGHTS

In order to characterize a given compound, a chemist must know its composition and molecular weight. From an analysis, one may determine the composition and, subsequently, the empirical formula. By one of several methods, the molecular weight may be found which may be used along with the empirical formula to determine the molecular formula. Of course, because of isomerism, the organic chemist requires a knowledge of the structural formula too. This is acquired from a study of the physical and chemical properties, but is beyond the scope of this Appendix.

Problem: By analysis it is found that a compound has the composition C, 56.25%; H, 3.9%; O, 12.5%; Cl, 27.34%. What is the empirical formula of the compound?

Solution: To find the ratio of carbon, hydrogen, oxygen, and chlorine atoms in the compound, which is the empirical formula, divide the percentage of each element by its atomic weight.

$$\frac{56.25}{12} = 4.69 \text{ gram atoms of carbon}$$

$$\frac{3.9}{1} = 3.9 \text{ gram atoms of hydrogen}$$

$$\frac{12.5}{16} = 0.781 \text{ gram atom of oxygen}$$

$$\frac{27.34}{35.5} = 0.770 \text{ gram atom of chlorine}$$

To get this ratio in whole integers, as formulas are always expressed, divide each value by the smallest and bring up the quotients to the nearest set of whole numbers. Thus,

Carbon	*Hydrogen*	*Oxygen*	*Chlorine*
$\frac{4.69}{0.770} = 6.09$	$\frac{3.9}{0.770} = 5.07$	$\frac{0.781}{0.770} = 1.01$	$\frac{0.770}{0.770} = 1.0$

that is,

$$(C_{4.69}H_{3.9}O_{0.781}Cl_{0.770})_n = (C_{4.69/0.770}H_{3.9/0.770}O_{0.781/0.770}Cl_{0.770/0.770})_n$$
$$= (C_{6.09}H_{5.07}O_{1.01}Cl_{1.0})_n \text{ or } (C_6H_5OCl)_n$$

The small discrepancies between the values 6.09, 5.07, 1.01 and the integers 6, 5, and 1, respectively, are due to errors in the experimental analysis.

Sometimes a ratio will be obtained such as 1.66:3.33:1. This cannot be placed equal to 2:3:1 because that would represent too large an error in the analysis. Instead, multiply the ratio by a small integer, such as 2, 3, 4, etc., until a ratio of nearly whole numbers is found. Here, for example,

$$_2(C_{1.66}H_{3.33}O_1) = C_{3.32}H_{6.66}O_2$$

$$_3(C_{1.66}H_{3.33}O_1) = C_{4.98}H_{9.99}O_3$$

The latter ratio is near enough to be considered as 5:10:3, or $C_5H_{10}O_3$.

Most organic compounds consist of two or more of the ten elements, carbon, hydrogen, oxygen, nitrogen, sulfur, phosphorus, and the halogens. The percentages of the various elements are found in the following manner: in most cases, carbon is converted into carbon dioxide, hydrogen into water, nitrogen into ammonia or nitrogen gas, sulfur into barium sulfate, phosphorus into an insoluble phosphate, halogen into silver halide, and oxygen is usually found by difference. The illustration below will show how this device may be used to determine the empirical formula of a compound.

Problem: A 0.220-g. sample of a compound which contained carbon, hydrogen, and oxygen gave upon analysis 0.6179 g. of CO_2 and 0.124 g. of H_2O. What is the empirical formula of the substance?

Solution: From their formulas, one knows that 12/44ths of the weight of CO_2 (mol. wt. = 44) is due to carbon, and 2/18ths of the weight of H_2O (mol. wt. = 18) is due to hydrogen. Hence,

$$\frac{12}{44} \times 0.6179 = 0.1685 = \text{weight of the carbon in the sample}$$

$$\frac{2}{18} \times 0.124 = 0.0138 = \text{weight of the hydrogen in the sample}$$

Therefore, the weight of oxygen in the sample is 0.220 − (0.1685 + 0.0138) = 0.038 g. From these weights, the composition of the compound may be calculated.

$$\%\ \text{carbon} = \frac{0.1685}{0.220} \times 100 = 76.6$$

$$\%\ \text{hydrogen} = \frac{0.0138}{0.220} \times 100 = 6.27$$

$$\%\ \text{oxygen} = \frac{0.038}{0.220} \times 100 = 17.3,\ \text{or}\ 100 - (76.6 + 6.27) = 17.13$$

If one wanted the empirical formula, these last operations would not be necessary, for they were, in effect, setting up a ratio of the elements by weight. If one divides the weights of carbon, hydrogen, and oxygen by the corresponding atomic weights and proceeds as above, he will get the ratio of gram atoms in the compound. Thus,

$$\begin{aligned} C_{0.1685/12}H_{0.0138/1}O_{0.038/16} &= C_{0.014}H_{0.0138}O_{0.00238} \\ &= C_{0.014/0.00238}H_{0.0138/0.00238}O_{0.00238/0.00238} \\ &= C_{5.9}H_{5.9}O_1 \end{aligned}$$

Hence, the empirical formula is C_6H_6O. From this formula, the theoretical percentages of carbon, hydrogen, and oxygen are computed to be 76.6, 6.38, and 17.0, respectively.

One may wish to determine the percentage errors in the analysis. From the formula for percentage error,

$$\%\ \text{error} = \frac{\text{difference between true and experimental value}}{\text{true value}} \times 100$$

$$\%\ \text{error in carbon analysis} = \frac{76.6 - 76.6}{76.6} \times 100 = 0$$

$$\%\ \text{error in hydrogen analysis} = \frac{6.38 - 6.27}{6.38} \times 100 = 1.37$$

$$\%\ \text{error in oxygen (by difference)} = \frac{17.3 - 17.0}{17.0} \times 100 = 1.76$$

Problem: A compound containing sulfur was analyzed and a sample weighing 0.22 g. gave 0.298 g. of $BaSO_4$. What percentage of sulfur did the compound contain?

Solution: To determine the percentage of sulfur, one must know the weight of sulfur in the compound. According to the formula of $BaSO_4$ (mol. wt. 233.4) 32/233.4 parts of the weight of $BaSO_4$ is due to sulfur. Therefore,

$$\frac{32}{233.4} \times 0.298 = 0.041 \text{ g.}$$

is the weight of sulfur in the precipitated barium sulfate. The percentage of sulfur in the sample is, then,

$$\frac{0.041}{0.22} \times 100 = 18.6\%$$

Problem: A gas is analyzed having the following composition: C, 81.8%; H, 18.2%. If 369 ml. measured at 22°C. and 748 mm. pressure weigh 0.66 g., what is its molecular formula?

Solution: To get the molecular formula, one needs the molecular weight and the ratio of gram atoms of carbon to hydrogen. The molecular weight can be obtained by determining the weight of 1 mole of gas at standard conditions; hence, one corrects the measured volume of gas to standard conditions by use of the gas law.

$$\frac{P_1V_1}{T_1} = \frac{P_2V_2}{T_2}$$

First, list the known values; then rearrange the equation to solve for the unknown quantity; and finally make the substitutions.

Thus,

$P_1 = 748$ mm. $\quad P_2 = 760$ mm.

$T_1 = 22°C. = 295°K.$ $\quad T_2 = 273°K.$

$V_1 = 369$ ml. $\quad V_2 = ?$

$$\frac{P_1V_1}{T_1} = \frac{P_2V_2}{T_2} \quad \text{or} \quad V_2 = \frac{T_2}{T_1} \times \frac{P_1}{P_2} \times V_1$$

Therefore,

$$V_2 = \frac{273}{295} \times \frac{748}{760} \times 369 = 336 \text{ ml.}$$

Since 336 ml. weigh 0.66 g., 22,400 ml. would weigh, according to the ratio,

$$\frac{\text{wt.}}{22{,}400} = \frac{0.66}{336}$$

$$\text{wt.} = 44 \text{ g.} = \text{the mol. wt.}$$

One knows that 81.8% of 44 is the weight of carbon and that 18.2% of 44 is the weight of hydrogen. When the weights of carbon and hydrogen are divided by their respective atomic weights, one gets the number of gram atoms of each element present in 1 mole of the compound.

Thus,

$$\frac{0.818 \times 44}{12} = 3.00 \text{ gram atoms of carbon}$$

$$\frac{0.182 \times 44}{1} = 8 \text{ gram atoms of hydrogen}$$

The molecular formula is then, C_3H_8.

Problem: A substance of molecular weight 180 has a composition of C, 40%; H, 6.67%; O, 53.33%. What is its molecular formula?

Solution: As above, the percentage of each element multiplied by 180 gives the weight of that element in the compound per mole. Then, the weight divided by the atomic weight will yield the number of gram atoms per mole, or atoms per molecule. Accordingly,

$$\frac{0.40 \times 180}{12} = 6 \text{ gram atoms of carbon}$$

$$\frac{0.0667 \times 180}{1} = 12 \text{ gram atoms of hydrogen}$$

$$\frac{0.5333 \times 180}{16} = 6 \text{ gram atoms of oxygen}$$

The molecular formula is then, $C_6H_{12}O_6$.

Molecular weights. The Victor Meyer method is one of the common methods of determining the molecular weights of organic liquids. When a weighed amount of the liquid is vaporized, the volume of air that is displaced is assumed to be equal to the volume of the vapor.

Problem: In the Victor Meyer method of determining molecular weights, a sample weighing 0.152 g. displaced 54.9 ml. of air over water at 25° and 738.5 mm. pressure (the vapor pressure of water at 25° is 23.5 mm.). What is the molecular weight of the compound?

Solution: The gas law equation, $PV = nRT$, is used, where n is the number of moles of compound and R is the gas law constant; in this case:

$V = 54.9$ ml.

$T = 25°\text{C.} = 298°\text{K.}$

$R = 82.1$ ml.-atmos.

$n = 0.152/\text{mol. wt.}$

P = total pressure less the vapor pressure of water, in atmospheres

$$= \frac{738 - 23.5}{760} = \frac{715}{760} \text{ atmos.}$$

$$PV = nRT = \frac{\text{wt.} \times RT}{\text{mol. wt.}}, \text{ or when rearranged, mol. wt.} = \frac{\text{wt.} \times RT}{PV}$$

$$\text{mol. wt.} = \frac{0.152 \times 82.1 \times 298 \times 760}{715 \times 54.9} = 72$$

Molecular weights of substances are also determined by ebullioscopic (boiling-point elevation) and cryoscopic (freezing-point lowering) methods. Both involve the same principles. For solids, a common practice is to measure the depression in the melting point of camphor. Camphor (m.p. 179°) is chosen because it has a large freezing-point depression constant of 39.7° (depression per mole of solute dissolved in 1000 g. of camphor). If *d* is the decrease in the m.p. temperature in degrees C., *w* is the weight of the sample, and *g* is the weight of camphor, then the molecular weight *M* can be calculated from the formula

$$M \quad \frac{39.7\, w \cdot 1000}{g \cdot d}$$

Simple substitution can be made in this equation for a given problem and need not be illustrated.

Functional group analyses. Most quantitative analyses are based on some reaction which is characteristic for a functional group present in the compound. For instance, the amount of a given aldehyde in a sample may be determined by weighing the amount of cuprous oxide that is precipitated from Fehling's solution, or the amount of 2,4-dinitrophenylhydrazone that is precipitated from the reagent solution. The amount of primary amine in a sample may be obtained by determining the volume of nitrogen gas liberated upon treatment with excess nitrous acid. Such practice is very prevalent and may be illustrated by a couple of examples. These analyses are usually done volumetrically—i.e., involve titrations—and several examples are given in Section A-4b.

Problem: A sample of a mixture of ethyl alcohol and acetaldehyde, weighing 0.535 g., precipitated 1.2 g. of cuprous oxide from Fehling's solution. What was the percentage of aldehyde in the mixture?

Solution: To find the percentage of aldehyde in the mixture, one must know the weight of aldehyde there. From the equation for the reduction of Fehling's solution with an aldehyde

$$5OH^- + RCHO + 2Cu^{++} \rightarrow Cu_2O + RCOO^- + 3H_2O$$

it is observed that 1 mole of aldehyde will produce 1 mole or 143.2 g. of cuprous oxide. Since the molecular weight of acetaldehyde is 44, one can set up the ratio for the weight of acetaldehyde

$$\frac{\text{wt.}}{44} = \frac{1.2}{143.2}, \qquad \text{wt.} = 0.369 \text{ g.}$$

Therefore, the weight is found to be 0.369 g. and this amount of aldehyde was present to precipitate the 1.2 g. of cuprous oxide. The percentage of aldehyde in the sample, then, is

$$100 \times \frac{0.369}{0.535} = 69\%$$

Problem: A solution weighing 10 g. and containing pentene was treated with bromine. The solvent was of a type which does not react with bromine. It was found that 14 g. of bromine had reacted with the pentene. What was the percentage of pentene in the solution tested?

Solution: To determine the percentage of pentene in the solution one must know the weight of pentene present. If one can find out how many moles of bromine reacted, he will know the number of moles of pentene that reacted, since bromine and pentene react mole for mole.

$$14/160 = 0.0875 \text{ mole of bromine} = 0.0875 \text{ mole of pentene.}$$

Therefore, 0.0875 × 70 = 6.12 g. of pentene (mol. wt. = 70). Hence, the percentage of pentene in the 10-g. sample is

$$\frac{6.12}{10} \times 100 = 61.2\%$$

EXERCISES

1. Calculate the weight of 1 l. of ethane gas at 0° and 760 mm., and at 30° and 700 mm. *Ans.* 1.34 g.; 1.11 g.

2. Calculate the volume of 12 g. of ethane at 35° and 750 mm. pressure. *Ans.* 10.2 l.

3. Calculate the empirical formulas of the following compounds from the percentage compositions:

C	*H*	*O*	*N*	*S*	*Answer*
66.0	6.42	14.69	12.84		$(C_6H_7ON)_n$
41.9	4.65	18.6	16.28	18.6	$(C_6H_8SN_2)_n$
50.82	8.48	40.66			$(C_5H_{10}O_3)_n$

4. Quantitative analysis of an organic compound gave the following results:

wt. of sample = 0.200 g.
wt. of CO_2 = 0.627 g.
wt. of water = 0.256 g.

Calculate the empirical formula of the compound. *Ans.* $(CH_2)_n$.

5. An organic compound contains 85.75% carbon. What is the lowest molecular weight which can be assigned to the compound? *Ans.* 28 (14 cannot be considered since 12 + 4 H's = 16 is the lowest molecular weight possible for a compound of carbon).

6. An alcohol that was isolated from a plant gave the following analysis: C, 64.4%; H, 10.7%; O, 24.9% by difference. The molecular weight by the Rast method gave values between 127 and 132. What is the best molecular formula, and what is the theoretical percentage of composition? *Ans.* Mol. form. = $C_7H_{14}O_2$.

7. A compound which contained nitrogen was analyzed with the following result: 0.32 g. of the substance gave 32.5 ml. of nitrogen measured at 22° and 738 mm. Calculate the percentage of nitrogen in the compound. *Ans.* 11.4%.

8. How many milliliters of nitrogen, measured at 28° and 745 mm., may be obtained from 0.2 g. of a compound having the molecular formula C_7H_9N? *Ans.* 23.55 ml.

9. A sample containing aniline was treated with nitrous acid. The 0.247-g. sample gave 54 ml. of nitrogen at 27° and 745 mm. What percentage of aniline was in the sample? *Ans.* 81%.

10. A compound A has the composition: C, 46.6%; H, 8.73%; O, 31.1%; and N, 13.6%. When 16 mg. are dissolved in 343 mg. of camphor, the m.p. of the mixture is found to be 161°. What is the molecular formula of A? *Ans.* $C_4H_9O_2N$.

11. Calculate the volume of liquid bromine (sp. gr. 3.12) that would be required for reaction, by addition only, with 15 l. of propene at 25° and 745 mm. pressure. *Ans.* 30.8 ml.

12. A sample weighing 0.65 g. was reacted with excess 2,4-dinitrophenylhydrazine solution and 1.75 g. of the 2,4-dinitrophenylhydrazone was precipitated. Assuming a 100% precipitation of any butyraldehyde present, what percentage of butyraldehyde was there in the sample? *Ans.* 77%.

13. The silver salt of a dibasic acid was decomposed by heat. A sample of salt weighing 0.565 g. left a 0.384 g. residue of silver. What is the molecular weight of the acid? *Ans.* 104.

14. A 3.22-g. sample of glucose, when added to an excess of Fehling's solution and heated, precipitated 2.4 g. of cuprous oxide. What percentage of glucose was in the sample? *Ans.* 93.8%.

15. In the ammonolysis of methyl chloride, 70% of it is converted to methyl amine, 20% to dimethyl amine, 7% to trimethyl amine, and 3% to tetramethyl ammonium chloride (all percentages by weight). What volume of methyl chloride at 17° and 752 mm. pressure would be required to produce 20 g. of methylamine hydrochloride according to these yields? *Ans.* 6.1 l.

16. A 9.2-g. sample of a mixture of ethanol and ethane are reacted with excess sodium and 224 ml. of hydrogen STP are collected. What is the percentage of alcohol in the mixture? *Ans.* 10%.

17. A 4.28-g. sample of a monohydric alcohol liberated 800 ml. of hydrogen gas, STP, when treated with metallic sodium. What is the molecular weight of the alcohol? *Ans.* 60.

18. A 0.2-g. sample of a compound whose molecular formula is $C_6H_{10}O_2$ gave 43.9 ml. of methane, STP upon reaction with methyl magnesium iodide. How many active hydrogen atoms are present in the compound? *Ans.* 1.

19. An organic compound contains 11% bromine. A sample weighing 0.24 g. would give what weight of silver bromide in an analysis? *Ans.* 0.062 g.

20. A liquid A has the composition: C, 40%; H, 6.66%; and O, 53.3%. A sample weighing 0.32 g. gave 172.7 ml. of vapor at 120° and 750 mm. pressure. What is the molecular formula of A? *Ans.* $C_2H_4O_2$.

21. A sample of an organic compound weighing 0.186 g. was analyzed for nitrogen by the Dumas method. It gave 24.94 ml. of nitrogen measured over water at 20°. If the barometer reading was 750 mm. and the vapor pressure of water at 20° was 17.5 mm., calculate the percentage of nitrogen in the sample. *Ans.* 15%.

A-3 STOICHIOMETRY

Probably the most important quantitative procedure in chemistry is stoichiometry. This is the use of balanced equations for determining quantity relationships between chemicals involved in chemical reactions. For example, the balanced equation

$$2KClO_3 \rightarrow 2KCl + 3O_2$$

states that for every 2 moles of potassium chlorate reacting, 2 moles of potassium chloride plus 3 moles of oxygen are produced, or that along with each mole of potassium chloride produced $1\frac{1}{2}$ moles of oxygen are produced simultaneously, or that to produce 1 mole of oxygen by this reaction, there is required $\frac{2}{3}$ mole of potassium chlorate. Of course, the relationships between weight, molecular weight, and number of moles leads to the weights of substances involved.

One important point is that the units of quantity for the substances concerned may be varied for convenience. For instance, in the reaction of bromine with ethane, gases and liquids are involved.

$$\begin{array}{cccc}
C_2H_{6\,gas} + & 2Br_{2\,liq.} & \rightarrow C_2H_4Br_{2\,liq.} + & 2HBr_{gas} \\
\text{1 mole} & \text{2 moles} & \text{1 mole} & \text{2 moles} \\
\text{30 g.} & \text{320 g.} & \text{188 g.} & \text{162 g.} \\
\text{22.4 l.} & 320/3.12 = \text{102.6 ml.} & & \text{44.8 l.}
\end{array}$$

According to this equation, 1 mole of ethane and 2 moles of bromine react to give 1 mole of dibromoethane plus 2 moles of hydrogen bromide. These quantities could be expressed in units of weight as indicated in the second row or, what is more convenient in this case, in units of volume (on the basis of Avogadro's law for the gases and from densities for the liquids). Furthermore, the units employed need not be the same for all substances. For example, one can say that 22.4 l. of ethane, STP, react with 102.6 ml. of liquid bromine to give 188 g. of dibromoethane plus 2 moles of hydrogen bromide. The only condition to be met is that when a ratio is set up, the same units must be used for any given substance. To illustrate, if it were desired to calculate the amount of bromine that would react with 15 g. of ethane according to this equation, a ratio can be set up as follows:

$$\frac{15}{30} = \frac{X}{\text{2 moles}} = \frac{Y}{\text{320 g.}} = \frac{Z}{\text{102.6 ml.}}$$

where the units of X, Y, and Z are the same as their respective denominators, or moles, grams, and milliliters, respectively. Similarly, if starting with 20 l. of ethane, STP, one could determine the quantity of HBr liberated by the ratio:

$$\frac{\text{20 l.}}{\text{22.4 l.}} = \frac{X}{\text{2 moles}} = \frac{Y}{\text{162 g.}} = \frac{Z}{\text{44.8 l.}}$$

where the units of X, Y, and Z are moles, grams, and liters, respectively.

Now the important feature about organic reactions is that very few take place strictly according to a single chemical equation. For example, when 2 moles of bromine and 1 mole of ethane are reacted, several products are formed rather than the single one indicated in the above equation. Two dibromoethanes would be produced in addition to small amounts of monobromoethane, tribromoethane, and trace amounts of tetra-, penta-, and hexabromoethane. These other products which are not wanted at this time are referred to as *side products* and the reactions through which they arise are called *side reactions*. Obviously, when it is desired to prepare a certain compound, a chemist is interested in converting all of his starting material into the desired product according to the respective equation, and he expresses the efficiency of this process in terms of per cent yield.

Thus, when a chemical reaction is expressible by a chemical equation, the amount of product indicated by the equation is the theoretical yield. It is the maximum amount of product obtainable from a given amount of starting material by means of a chosen reaction. Accordingly, the per cent yield is determined by the expression:

$$\% \text{ yield } \frac{\text{actual yield} \times 100\%}{\text{theoretical yield}}$$

where the units of actual and theoretical yield are the same. This can be illustrated by several problems.

Problem: What is the per cent yield of decane if 15.1 g. of *n*-bromopentane are reacted with excess sodium metal by a Wurtz reaction and 6.5 g. of decane are isolated?

Solution: According to the relationship above, in order to compute the per cent yield, one must know the actual and theoretical yields. The actual yield is given and the theoretical yield may be calculated through stoichiometry, making use of the chemical equation for the reaction:

$$\underset{\substack{2\text{ moles}\\ 2 \times 151 = 302\text{ g.}}}{2\text{Br—C}_5\text{H}_{11}} + 2\text{Na} \rightarrow \underset{\substack{1\text{ mole}\\ 142\text{ g.}}}{\text{C}_{10}\text{H}_{22}} + 2\text{NaBr}$$

It is seen that 302 g. of bromopentane produce 142 g. of decane; hence, the weight of decane, X, obtainable from 15.1 g. of bromopentane is, according to the ratio:

$$\frac{15.1}{302} = \frac{X}{142}, \qquad X = 7.1\text{ g.}$$

This is the theoretical yield or maximum amount obtainable from 15.1 g. of bromopentane through this reaction. The per cent yield then is found by using the expression above.

$$\% \text{ yield} = \frac{\text{actual yield} \times 100\%}{\text{theoretical yield}}$$

$$= \frac{6.5 \times 100\%}{7.1} = 91.5\%$$

Problem: What is the per cent yield in the production of acetaldehyde from acetylene if from the hydration of 3.02 l. of acetylene, measured at 2 atmos. and 95°, 7.8 g. of acetaldehyde are recovered?

Solution: Again, the actual yield is known; so to calculate the per cent yield one determines the theoretical yield from the chemical equation for the reaction.

$$\underset{\substack{22.4\text{ l.}\\ 26\text{ g.}}}{\text{C}_2\text{H}_2} + \text{H}_2\text{O} \rightarrow \underset{44\text{ g.}}{\text{CH}_3\text{CHO}}$$

The theoretical yield of acetaldehyde is based upon the amount of acetylene available for reaction, which is 3.02 l. at 2 atmos. pressure and 95°. Quantities indicated by chemical equations are for standard conditions, so this volume of acetylene must be corrected first for pressure and temperature for adjustment to standard conditions. To do this, one uses the gas law, for which

$V_1 = 3.02\text{ l.}$ $\qquad V_2 = ?$

$P_1 = 2\text{ atmos.}$ $\qquad P_2 = 1\text{ atmos.}$

$T_1 = 95°\text{C.} = 368°\text{K.}$ $\qquad T_2 = 273°\text{K.}$

Rearranging the gas law to solve for V_2, one has:

$$V_2 = \frac{T_2}{T_1} \times \frac{P_1}{P_2} \times V_1 = \frac{273}{368} \times \frac{2}{1} \times 3.02 = 4.48 \text{ l.}$$

Then, by stoichiometry and the chemical equation, 22.4 l. of acetylene, STP, give 44 g. of acetaldehyde, so 4.48 l. will give X grams of acetaldehyde in the ratio:

$$\frac{4.48}{22.4} = \frac{X}{44}$$

$$X = 8.8 \text{ g.}$$

Therefore, the per cent yield is

$$\frac{7.8}{8.8} \times 100\% = 88.6\%$$

There are two important practical uses of per cent yield that students often have difficulty in distinguishing. One is quite simple and is the determination of the amount of product which will be produced when the per cent yield for the reaction is already known to be less than 100%. The second situation is a computation of the amount of starting material required for the preparation of a given quantity of product when the per cent yield is known to be less than 100%. These two problems may be illustrated by several examples.

Problem: What weight of pentene will be produced by the dehydration of 60 g. of pentanol if the per cent yield is only 82%?

Solution: The same relationship can be used between per cent, actual, and theoretical yields, with per cent yield being known in this case instead of actual yield. Again, the theoretical yield is determined by means of stoichiometry and the chemical equation for the reaction:

$$\underset{88\text{ g.}}{CH_3CH_2CH_2CH_2CH_2OH} + H_2SO_4 \rightarrow \underset{70\text{ g.}}{CH_3CH_2CH_2CH{=}CH_2} + H_2O\cdot H_2SO_4$$

Sixty grams of pentanol will yield X g. of pentene according to the ratio

$$\frac{60}{88} = \frac{X}{70}$$

$$\therefore X = 47.7 \text{ g.}$$

This is the theoretical yield; therefore, the actual yield will be

$$\begin{aligned} \text{Actual yield} &= \%\text{ yield} \times \text{theoretical yield} \\ &= 82\% \times 47.7 \text{ g.} \\ &= 0.82 \times 47.7 \text{ g.} \\ &= 39.1 \text{ g.} \end{aligned}$$

It is seen that the actual yield is obtained by multiplying the theoretical yield by a number less than unity whenever the per cent yield is less than 100%.

Problem: If the yield from a Wurtz reaction were 65%, what weight of butyl bromide would be required to produce 4.56 g. of *n*-octane?

Solution: The equation for the reaction is:

$$2CH_3(CH_2)_2CH_2Br + 2Na \rightarrow CH_3(CH_2)_6CH_3 + 2NaBr$$

Two approaches to this type of problem are commonly used, the first being as follows: 4.56 g. of *n*-octane are to be produced with the per cent yield being 65%, so that 4.56 g. must represent 65% of the weight that would have been produced at 100% yield. That is

$$4.56\text{ g.} = 0.65\ W$$

$$\text{Wt.} = \frac{4.56}{0.65} = 7.02\text{ g.}$$

Now, one can calculate in the usual fashion what weight of butyl bromide would have been necessary to produce 7.02 g. of octane at 100% yield. From the chemical equation and stoichiometry, the weight sought is obtained from the ratio:

$$\frac{X}{274} = \frac{7.02}{114}$$

$$X = 16.9\text{ g.}$$

The second way to consider the problem might be referred to as a *correction-factor method*. It consists of calculating the required weight of material on a basis of 100% yield; then making an adjustment for the fact that the yield is less than 100 by multiplying by an appropriate factor. Logic dictates that since the reaction is less than 100% efficient, a greater amount of starting material is necessary than indicated by the stoichiometry of the chemical equation; therefore the correction factor must be greater than unity. In this problem, to produce 4.56 g. of *n*-octane at 100% yield, the weight of butyl bromide necessary is, from the ratio,

$$\frac{4.56}{114} = \frac{X}{274}, \qquad X = 10.96\text{ g.}$$

Since the yield is only 65%, one must start with $10.96\ (\frac{100}{65}) = 16.9$ g. That is, the correction factor is always divided by the per cent yield. So, the two problems that arise when per cent yield is already known to be less than 100% are (1) to calculate what the actual yield will be from a given weight of starting material, and (2) to calculate the weight of starting material required to produce a desired quantity of product. These can be treated in the usual fashion as if the per cent yield were 100, but then the answer is multiplied by

$$\frac{\text{given \% yield}}{100}$$

in the first case, and by

$$\frac{100}{\text{given \% yield}}$$

in the second case. The second case can be illustrated by another problem.

Problem: What weight of sodium propionate would be required to produce 1.12 l. of ethane, STP, if one assumes the reaction can be carried out with an 80% yield?

Solution: The chemical equation for the reaction is

$$\underset{96\text{ g.}}{CH_3CH_2CO_2Na} + NaOH \rightarrow \underset{\substack{30\text{ g.}\\22.4\text{ l.}}}{C_2H_6} + Na_2CO_3$$

As suggested above, first find the answer for 100% yield; then multiply by

$$\frac{100}{\text{given \% yield}}$$

which is 100/80 here. The stoichiometric ratio for the weight required for 100% yield would be

$$\frac{X}{96} = \frac{1.12}{22.4}, \qquad X = 4.8 \text{ g.}$$

Then, $4.8(\frac{100}{80}) = 6$ g. Again, the second approach is not as quick but is as follows:

$$1.12 \text{ l.} = 0.80\ V$$

where V is the volume that would have been produced were the per cent yield of 100 realized. Hence, $V = 1.4$ l. Now, to produce 1.4 l. at 100% yield would require sodium propionate according to the ratio:

$$\frac{X}{96} = \frac{1.4}{22.4}, \qquad X = 6 \text{ g.}$$

Finally, one more application of per cent yield arises when successive reactions are being used. For instance, in a sequence of reactions, A → B → C, if each step takes place at less than 100% yield, obviously to produce 1 mole of C will require more than 1 mole of B, and in turn a still greater factor than 1 mole of A. For illustration, look at the next problem.

Problem: What volume of ethane would be required to produce 50 g. of *n*-butane by monobromination of ethane followed by a Wurtz reaction using the resulting ethyl bromide, if the bromination takes place with a 90% yield and the Wurtz reaction with an 85% yield?

Solution: When using a sequence of reactions, it is more convenient to work with moles until the last step when number of moles can be converted into the units in which the answer is expressed. Therefore, for the two reactions

$$\underset{\substack{30\text{ g.}\\22.4\text{ l}}}{C_2H_6} + Br_2 \rightarrow C_2H_5Br + HBr$$

and

$$2C_2H_5Br + 2Na \rightarrow \underset{58\text{ g.}}{C_4H_{10}} + 2NaBr$$

one can apply the correction-factor method to adjust for the per cent yield. For the second equation, the number of moles required to produce 50 g. of *n*-butane at 100% yield is

$$\frac{X}{2} = \frac{50}{58}, \qquad X = 1.724 \text{ moles}$$

Then

$$1.724\left(\frac{100}{85}\right) = 2.03 \text{ moles}$$

Now, from the first equation, 1 mole of ethane produces 1 mole of ethyl bromide at 100% yield; so, to produce 2.03 moles at 90% yield would require

$$2.03\left(\frac{100}{90}\right) = 2.26 \text{ moles}$$

At standard conditions, this would be

$$2.26 \times 22.4\ \text{l.} = 50.6\ \text{l. of ethane} \quad (\textit{Ans.})$$

Notice particularly that, in finding the quantity of original starting material, one starts with the last chemical equation and works his way back to the first chemical equation.

Problem: What volume, STP, of chlorine gas would be required in the production of 100 g. of vinylacetylene by trichlorination of methane, conversion of the chloroform to acetylene by reaction with zinc dust, and dimerization of the acetylene, if each reaction takes place with a 76% yield?

Solution: The chemical equations involved are:

$$CH_4 + 3Cl_2 \rightarrow CHCl_3 + 3HCl \qquad (1)$$

$$2CHCl_3 + 3Zn \rightarrow C_2H_2 + 2ZnCl_2 \qquad (2)$$

$$2C_2H_2 \rightarrow \underset{52\text{ g.}}{CH_2{=}CH{-}C{\equiv}CH} \qquad (3)$$

One hundred grams of vinylacetylene is 100/52 = 1.925 moles. From reaction (3), one observes that this would take 2 × 1.925 moles of acetylene at 100% yield, or at 76% yield:

$$2 \times 1.925\left(\frac{100}{76}\right) = 5.07\ \text{moles}$$

To produce this quantity of acetylene according to reaction 2 it would take 2 × 5.07 moles of chloroform at 100% yield. Hence, at 76% yield it would require

$$2 \times 5.07\left(\frac{100}{76}\right) = 13.35\ \text{moles}$$

Then, from the first equation, to produce 13.35 moles of chloroform at 100% yield takes 3 × 13.35 moles of chlorine; so at 76% yield, the necessary number of moles of chlorine is

$$3 \times 13.35\left(\frac{100}{76}\right) = 52.75\ \text{moles}$$

Therefore, what was initially sought, namely the volume of chlorine which is necessary in the production of 100 g. of vinylacetylene by these successive reactions, is 52.75 moles, or 52.75 × 22.4 l. = 1.18 l., STP.

An incorrect step which many students attempt in these per cent yield problems is to correct for the shortage in yield by adding a certain percentage. For instance, if a reaction takes place with an 80% yield and a certain quantity of product is desired, one can calculate the required amount of starting material on a 100% yield basis, and then use the correction factor of 100/80. However, one cannot make the adjustment by simply adding 20% more. That is, one cannot calculate the required amount of starting material on a 100% yield basis and then take 20% more. This latter step is equivalent to using 120% of a certain quantity X and does not equal 100/80 times X. This becomes obvious when the per cent yield is much less than 100. For illustration, if the per cent yield is 50, then 150/100 = 1.5 is not the same as 100/50 = 2. The closer the per cent yield is to 100, the closer these two ratios become.

EXERCISES

1. If a batch of calcium carbide is 89% pure, what weight would be required to produce 17 l. of acetylene, STP? *Ans.* 54.7 g.

2. What volume of chloroform, density 1.49 g/ml, would be required to produce 1 l. of acetylene, STP? *Ans.* 7.16 ml.

3. What volume of ethylene STP should be obtained from 2 lb. of 95% ethanol (C_2H_5OH)? *Ans.* 420 l.

4. What volume of pure oxygen, STP, is required to burn 20 g. of ethane? *Ans.* 52.3 l.

5. If a saturated solution of calcium sulfate contains 0.17 mg. per 100 ml. of solution, what weight of sodium stearate would be necessary to soften 1 kl. of saturated calcium sulfate solution? *Ans.* 7.65 g.

6. What weight of aniline would be required to produce 90 g. of phenol if one assumes a 42% yield? *Ans.* 212 g.

7. What weight of calcium carbide would be required to produce 1 l. of acetylene measured at 0.5 atmos. pressure and 273° if the acetylene can be collected with only 80% efficiency and the calcium carbide is 70% pure? *Ans.* 1.28 g.

8. What volume of nitrogen gas, measured at 740 mm. pressure and 25° will be liberated if 0.15 g. of butylamine are treated with nitrous acid, and the N_2 collected in a 90% yield? *Ans.* 46.4 ml.

9. What weight of the phenylhydrazone could be produced from 17.2 g. of 3-pentanone if the per cent yield is 92%? *Ans.* 32.4 g.

10. What weight of butyric acid could be made from 12.3 g. of *n*-propyl bromide by forming a Grignard, carbonating the Grignard, and hydrolyzing the addition product, if the yield in each of the three steps is 90%? *Ans.* 6.4 g.

11. What weight of propionitrile would be required to produce 14.8 g. of propionic acid if the yield in the hydrolysis is assumed to be 88%? *Ans.* 12.5 g.

12. What weights of methyl ethyl ketone and methanol would be necessary to produce 47.2 g. of the methyl acetal, $CH_3—CH_2—C(OCH_3)_2—CH_3$ if the per cent yield is known not to exceed 70%? *Ans.* 41.1 g. ketone; 36.6 g. alcohol.

13. What weight of isopropylamine should be used to produce 36.9 g. of isopropyl bromide by reacting the amine with nitrous acid and the resulting alcohol with phosphorus tribromide, if the per cent yield in the first reaction is estimated to be 65% and that of the second reaction is 80%? *Ans.* 34.1 g.

A-4 VOLUMETRIC GROUP ANALYSES

Equivalent and Molecular Weights

a. Units of concentration. It is frequently desired to change the units of concentration, particularly from one used more in industry, per cent by weight, to one of those common in the laboratory, such as molarity, normality, or mole fraction.

Problem: An aqueous solution of ethyl alcohol, which contains 18% alcohol by weight, has a density of 0.974. Calculate the molarity of the alcohol in the solution and the mole fraction of the alcohol.

Solution: This problem is solved essentially on the basis of the definitions of the terms involved. Molarity is the number of moles of solute per liter of solution; mole fraction is the number of moles of solute divided by the total number of moles of all components in the solution including the solvent; and density is the mass per unit volume. Thus, if one takes a liter of solution, he can determine its total mass by substituting in the equation:

$$D = M/V$$

where D is the density, M is the mass, and V is the volume.

$$0.974 = M/1000; \quad \text{therefore, } M = 974 \text{ g.}$$

Since 18% of this mass is alcohol, one can calculate the weight of alcohol and, hence, the number of moles, m, of alcohol present.

$$\text{wt.} = 0.18 \times 974 = 175 \text{ g.}$$

and

$$m = \text{wt./mol. wt.} = 175/46 = 3.81 \text{ moles}$$

Therefore, the molarity is 3.81 M. If one subtracts the weight of the alcohol (175 g.) from the total weight, he obtains the weight of the water: 974 − 175 = 799 g. Thus, 799/18 moles of water = 44.3. The mole fraction of the alcohol is

$$\frac{3.81}{3.81 + 44.3} = 0.0791$$

Problem: What is the normality of a 60% acetic acid solution whose specific gravity is 1.06?

Solution: Again, by definition, the specific gravity is the density of the solution relative to that of water at the same temperature. If one assumes the density of water at this temperature is 1.0, then the density of the acetic acid solution is 1.06. Thus, in 1000 ml. of solution:

$$D = \text{wt.}/V \quad \text{or} \quad 1.06 = \text{wt.}/1000$$

$$\therefore \text{wt.} = 1060 \text{ g.}$$

Sixty per cent of this weight is due to acetic acid:

$$0.6 \times 1060 = 636 \text{ g.}$$

The normality, number of equivalents per liter, is then:

$$636/60 = 10.6 \text{ moles} = 10.6 \text{ eq.} = 10.6\,N.$$

EXERCISES

1. Calculate the normality of the following concentrated reagents:

Substance	*Per Cent by Weight*	*Density*	*Answer*
HCl	36.5	1.18	11.8
H_2SO_4	96	1.84	36
KOH	40.1	1.40	10
NH_4OH	30.4	0.895	16
HNO_3	70.33	1.42	15.9

2. What weight of solid sodium hydroxide and what volume of water must be used

to make 350 g. of: (a) a 10% solution by weight of sodium hydroxide; (b) a solution in which the mole fraction of NaOH is 0.1?

Ans. (a) 35 g. NaOH and 315 ml. H_2O;
(b) 69.3 g. NaOH and 281 ml. H_2O.

3. What weight of acetic anhydride should be added to 75 g. of 92% acetic acid so that, upon hydrolysis of the acetic anhydride, the concentration of acetic acid will be 100%? *Ans.* 34 g.

b. Titrations. One of the most useful pieces of information to aid in the elucidation of the structure of a compound is a knowledge of its equivalent weight with respect to some reaction; such as acid-base neutralization, hydrolysis, addition of halogen, oxidation or reduction, or liberation of a gas. The reaction that is chosen depends upon the nature and properties of the compound. Usually a titration is performed which is really a form of volumetric group analysis.

The fundamental principle of titration is the addition of a standardized solution to a complementary solution whose concentration is not known, until an equal number of equivalents have been added (the end point), as indicated by some visible change. Since the volume and concentration of the standardized solution are known, one can calculate the number of equivalents added, which equals the number of equivalents of sample in the unknown solution. In the solution of such problems the student will find it expedient if he works in terms of number of equivalents and number of moles. For this reason, a definition of several symbols that will be used in this appendix for working out such problems are:

m = number of moles
mol. wt. = molecular weight
M = molarity
V = volume in ml.

n = number of equivalents
eq. wt. = equivalent weight
N = normality
wt. = weight

It can be shown that:

$$m = \frac{M \times V}{1000}; \quad n = \frac{N \times V}{1000}; \quad \text{eq. wt.} = \frac{\text{wt.}}{n}$$

Problem: What is the equivalent weight of an acid, if for 0.231 g. of acid there are required 26.2 ml. of 0.1 N NaOH to reach a phenolphthalein end point?

Solution: Knowing the weight of acid, one can determine its equivalent weight by calculating the number of equivalents of acid present. This can be calculated from the normality and volume of alkali required to neutralize the acid. Thus, at the end point,

$$n_{\text{acid}} = n_{\text{base}} = \frac{N_b \times V_b}{1000} = \frac{0.1 \times 26.2}{1000} = 0.00262$$

Therefore,

$$\text{eq. wt.} = \frac{0.231}{0.00262} = 88.$$

Problem: What is the molecular weight of an ester of a dicarboxylic acid if, after hydrolysis of 0.78 g. in 50 ml. of 1.0 *N* NaOH, 34.8 ml. of 1.15 *N* HCl are required to neutralise the unreacted NaOH?

Solution: To get the molecular weight one must know the number of moles of ester that there are in 0.78 g. of the ester. Since the ester is one from a dicarboxylic acid, its molecular weight will be equal to twice its eq. wt., i.e., 1 mole of ester will hydrolyze and liberate two equivalents of acid. Therefore, one must find the number of equivalents of acid that were liberated. The number of equivalents of alkali used for the hydrolysis is equal to the number of equivalents liberated in the hydrolysis plus the number of equivalents of acid added in the titration. Two of these values are known, and the third may be calculated:

$$n_b = \frac{50 \times 1}{1000} = 0.05$$

$$n_a \text{ (titer)} = \frac{34.8 \times 1.15}{1000} = 0.04$$

$$n_a \text{ (organic)} = 0.05 - 0.04 = 0.01$$

Therefore, the number of moles of ester = 0.01/2 = 0.005.

$$\text{mol. wt.} = \frac{\text{wt.}}{m} = \frac{0.78}{0.005} = 156$$

Problem: What is the molecular weight of an amine, if 0.078 g. of it produce 59.9 ml. of nitrogen gas by the action of nitrous acid, measured at 25°C. and 738 mm. pressure, and one assumes the yield of nitrogen to be 95%?

Solution: To get the molecular weight one must know the number of moles of amine there are in 0.078 g. From the equation for the reaction,

$$RNH_2 + HONO \rightarrow ROH + N_2 + H_2O$$

1 mole of nitrogen gas is liberated by 1 mole of the amine. Hence, calculate the number of moles of nitrogen gas, i.e., its volume at standard conditions. Since the yield was only 95%, then the volume of gas one would have obtained at 100% yield is:

$$\frac{59.9}{95} = \frac{V}{100}, \quad \text{hence } V = 63 \text{ ml.}$$

$$V_1 = 63 \text{ ml.} \qquad V_2 = ?$$

$$P_1 = 738 \text{ mm.} \qquad T_2 = 273\text{°K.}$$

$$T_1 = 25\text{°C.} = 298\text{°K.} \qquad P_2 = 760 \text{ mm.}$$

$$V = \frac{T_2}{T_1} \times \frac{P_1}{P_2} \times V_1$$

$$= \frac{273}{298} \times \frac{738}{760} \times 63 = 56 \text{ ml.}$$

The number of moles of nitrogen = number of moles of amine $= \frac{56}{22{,}400} = 0.0025.$

Therefore,

$$\text{mol. wt. amine} = \frac{0.078}{0.0025} = 31.2$$

Problem: What is the molecular weight of a trihydric alcohol if 0.46 g. of it is acetylated with acetic anhydride, and, at ice temperature, 15 ml. of 1 N NaOH are required to neutralize the liberated acid?

Solution: According to the equation for the acetylation,

$$R(OH)_3 + 3Ac_2O \rightarrow R(OAc)_3 + 3AcOH$$

we see that 3 moles of acetic anhydride react with 1 mole of the trihydric alcohol. To determine its molecular weight, one must know how many moles of alcohol there are in 0.46 g. This can be calculated from the number of moles, i.e., equivalents of acetic acid liberated. To get this, find out how many equivalents of alkali are required to neutralize the acid. Hence,

$$n_a = n_b = \frac{N_b \times V_b}{1000} = \frac{1 \times 15}{1000} = 0.015$$

But for every three equivalents of acid, only 1 mole of alcohol reacted; therefore the number of moles of alcohol is 0.015/3 = 0.005, which will give the molecular weight as:

$$\frac{0.46}{0.005} = 92$$

Problem: How many OH groups are there in a polyhydric alcohol (mol. wt. 180) if 0.3 g. are acetylated with excess acetyl chloride, and 32.8 ml. of 0.254 N NaOH are required to neutralize the liberated HCl?

Solution: According to the general equation,

$$R(OH)_x + x\,AcCl \rightarrow R(OAc)_x + x\,HCl$$

x moles of acetyl chloride react with 1 mole of the alcohol containing x OH groups, with the liberation of x moles of HCl. Thus, if one can determine the number of moles, i.e., equivalents of HCl produced, he can compute the number of moles that are liberated when 1 mole of alcohol reacts; and therefore, calculate the number of equivalents of acid liberated as:

$$n_b = \frac{V_b \times N_b}{1000} = \frac{0.254 \times 32.8}{1000} = 0.00833 = n_a$$

That is, 0.00833 mole of HCl were produced. Now, the number of moles of alcohol reacting was

$$\frac{\text{wt.}}{\text{mol. wt.}} = m = \frac{0.3}{180} = 0.00167$$

Thus, the value of x in the equation is found from the ratio

$$\frac{0.00833}{0.00167} = \frac{x}{1}$$

$$x = 5.$$

c. Fat analyses. The principles involved in the above titration problems form the basis for the several types of fat analyses, such as the Reichert-Meissl number, the Polenske number, the saponification number, the iodine number, the acid value, etc.

Problem: What is the *acid value* of a fat if 26.9 ml. of 0.01 N KOH are required to neutralize a suspension of 0.24 g. of the fat in water?

Solution: The *acid value* is defined as the number of mg. of KOH required to neutralize the free fatty acid in one gram of fat. Thus, if one computes the volume of alkali that will react with 1 g. of fat, he can calculate the number of milligrams of KOH that are in solution. The volume of KOH to react with 1 g. of fat is found by the ratio:

$$\frac{26.9}{0.24} = \frac{V}{1}, \qquad V = \frac{26.9}{0.24} = 112 \text{ ml.}$$

The number of equivalents, hence, moles of KOH dissolved in this volume of 0.01 N solution is

$$n_b = \frac{0.01 \times 112}{1000} = 0.00112$$

The weight of KOH (mol. wt. 56.1), then, is

$$0.00112 \times 56.1 = 0.063 \text{ g.}$$

Therefore, the weight in milligrams is 63, which is the *acid value.*

Problem: How many grams of KOH would be required to neutralize a suspension in water of 250 g. of a fat whose *acid value* is 36?

Solution: From the definition of the *acid value*, one knows that 36 mg. of KOH will neutralize 1 g. of this fat. Hence, one may calculate the number of milligrams of KOH that will neutralize 250 g. Thus,

$$\frac{36}{1} = \frac{x}{250}$$

$$x = 36 \times 250 = 9000 \text{ mg.}$$

Therefore, the weight of KOH required is 9000 mg. or 9.0 g.

Problem: What is the *saponification number* of a fat if 31.6 ml. of 0.497 N KOH in ethanol are required in the hydrolysis of 1.8 g. of fat?

Solution: The *saponification number* of a fat is the number of milligrams of KOH required to saponify 1 g. of the fat. Here again one determines the volume of standardized alkali that would react with 1 g. of fat and then calculates the weight of KOH that is in solution. Since 31.6 ml. reacted with 1.8 g. of fat, the volume that would react with 1 g. of fat is

$$\frac{31.6}{1.8} = \frac{V}{1}$$

$$V = 17.55 \text{ ml.}$$

The number of equivalents, hence, the number of moles of KOH in solution is

$$n_b = \frac{17.55 \times 0.497}{1000} = 0.00873$$

Thus, the weight of KOH (mol. wt. 56.1) is

$$0.00873 \times 56.1 = 0.49 \text{ g. or } 490 \text{ mg.}$$

The latter figure is the *saponification number.*

Problem: What is the ***Reichert-Meissl number*** of glyceryl tributyrate?

Solution: It is to be realized that, normally, the *R-M number* will be small because only the carboxylic acids of 12 carbon atoms or less are volatile with steam, and only those of 4 or less carbon atoms are appreciably soluble in water. Moreover, natural fats contain only small percentages of these low-molecular-weight glycerides. The *R-M number* determines the water-soluble, steam-distillable fatty acids, while the *Polenske number* determines the water-insoluble, steam-distillable fatty acids obtained from 5 g. of the fat. The principles in the calculations will be the same. The *R-M number* is defined as the number of milliliters of 0.1 N KOH required to neutralize the water-soluble, steam-distillable fatty acids obtained from 5 g. of the fat. Since all of the acid liberated from the glyceryl tributyrate will be titrated, the *R-M number* will be unusually large. According to the definition, 5 g. of glyceryl tributyrate will be hydrolyzed. To determine the *R-M number* one must find out what volume of 0.1 N KOH will react with the liberated butyric acid. According to the equation,

$$C_3H_5(OOCR)_3 + 3H_2O \rightarrow C_3H_5(OH)_3 + 3RCOOH$$

each mole of ester will produce 3 moles of acid. The number of moles of ester is

$$\frac{\text{wt.}}{\text{mol. wt.}} = m = \frac{5}{302} = 0.01656$$

The number of moles of acid, hence number of equivalents of acid, is

$$3 \times 0.01656 = 0.0497.$$

This, then, equals the number of equivalents of alkali required for neutralization, or:

$$n_a = n_b = \frac{0.1\ V_b}{1000} = 0.0497$$

$$V_b = \frac{49.7}{0.1} = 497.$$

The *R-M number* is, therefore, 497.

Problem: What is the *Polenske number* of a fat, if it is found that 12.7 ml. of 0.087 N KOH are required to neutralize the water-insoluble, volatile acids obtained from 6.0 g. of fat.

Solution: Since the *Polenske number* is the volume of 0.1 N KOH required to neutralize the water-insoluble, volatile acids from 5 g. of fat, first compute the volume of alkali that would have been required for 5 g. of fat; then compute what volume of 0.1 N KOH is equivalent to the latter volume of 0.087 N KOH. The volume of 0.087 N KOH to be used for 5 g. of fat is

$$\frac{12.7}{6} = \frac{V}{5}$$

$$V = \frac{5 \times 12.7}{6} = 10.6 \text{ ml.}$$

The volume of 0.1 N KOH equivalent to 10.6 ml. of 0.087 N KOH is calculated from the relationship, $V_1N_1 = V_2N_2$, where the subscript 1 refers to the initial volume and concentration, and the subscript 2 to the final volume and concentration. Here, $V_1 = 10.6$, $N_1 = 0.087$, and $N_2 = 0.1$.
Therefore,

$$V_2 = \frac{V_1N_1}{N_2} = \frac{10.6 \times 0.087}{0.1} = 9.2 \text{ ml.}$$

The *Polenske number* is, then, 9.2.

Problem: What is the iodine number of α-palmitodilinolein?

Solution: The iodine number is defined as the weight of iodine that will react with 100 g. of the fat. Although iodine chloride or iodine bromide is frequently used as the iodinating agent, 1 mole of ICl is equivalent to 1 mole of iodine as seen by the equation:

$$HgCl_2 + 2I_2 \rightarrow HgI_2 + 2ICl$$

$$RCH{=}CHR + 2ICl \rightarrow RCHI{-}CHIR + Cl_2$$

Thus, one can work on the basis that iodine is the reactant. From the equation,

$$C_3H_5(OOCR)_3 + x\ I_2 \rightarrow \text{product},$$

the first step is to determine the number of moles of iodine that react with 1 mole of the fat. This will depend upon the number of ethylenic bonds present in the three acid radicals. Palmitic acid has no double bonds and linoleic acid has two. α-Palmitodilinolein thus has 4 double bonds per molecule, so x is 4. The number of moles of fat is

$$\frac{\text{wt.}}{\text{mol. wt.}} = m = \frac{100}{854} = 0.1171.$$

Therefore, the number of moles of iodine reacting is

$$4 \times 0.1171 = 0.468, \text{ and its weight is}$$

$$0.468 \times 254 = 119 \text{ g}.$$

The *iodine number* is then, 119.

Problem: How many ethylenic groups are there in a glyceride of molecular weight 878 which has an *iodine number* of 174?

Solution: From the definition of the *iodine number*, one knows that 174 g. of iodine will react with 100 g. of this glyceride. From the equation,

$$C_3H_5(OOCR)_3 + x\ I_2 \rightarrow \text{product},$$

x moles of iodine react with 1 mole of a glyceride which contains x double bonds. One can determine the number of moles of glyceride used and the number of iodine added. From the ratio of these two values, one can calculate x, the number of double bonds in the fat. Consequently, the number of moles of iodine is 174/254 = 0.685 and the number of moles of glyceride is 100/878 = 0.114. The ratio of the two values is thus 0.685/0.114 = 6. Hence, the number of double bonds in the glyceride is six.

EXERCISES

1. A neutral sample of crude ethyl acetate, weighing 2.4 g., was boiled with 50 ml. of 0.5 *N* alkali. The reaction product was back titrated and required 22.5 ml. of 0.1 *N* acid for neutralization. What was the percentage of ester in the sample?
Ans. 83.4%.

2. What volume of 1 *N* alkali will be neutralized by 5 g. of succinic acid?
Ans. 84.8 ml.

3. A certain monocarboxylic acid was titrated with 0.1 *N* KOH. A 0.21-g. sample required 17.2 ml. of the alkali. What is the molecular weight of the acid?
Ans. 122.

4. What is the molecular weight of an amide, if, after 0.61 g. is hydrolysed and the

liberated amine is distilled into 100 ml. of 0.1 *N* HCl, 38.4 ml. of 0.13 *N* NaOH are required to neutralize the excess HCl? *Ans.* 122.

5. What is the percentage yield in a Rosenmund reduction of 0.46 g. of propionyl chloride, if the liberated HCl is collected in 100 ml. of 0.1 *N* NaOH, and 45 ml. of 0.12 *N* HCl are required to neutralize the excess alkali? *Ans.* 92.5%.

6. In the ammonolysis of propyl bromide, a mixture of mono-, di-, and tripropyl amine is obtained. A 0.934-g. sample of the mixture was titrated with 0.50 *N* HCl and 34.6 ml. were required for neutralization. A 2-g. sample of the reaction product was reacted with benzenesulfonyl chloride and the liberated HCl trapped in 50 ml. of 1 *N* NaOH. It was found that 16.1 ml. of 1.23 *N* HCl were required to neutralize the excess alkali. Then a 0.151-g. sample of the mixture of amines was reacted with nitrous acid. The liberated nitrogen was collected at 25° over water ($V.P._{H_2O}$ = 23.5 mm.) at 740 mm. pressure, and the volume was found to be 53.2 ml. What were the percentages by weight of primary, secondary, and tertiary amine in the mixture? *Ans.* 80.2%, P; 14.8%, S; 5.02%, T.

7. How many OH groups are there in a polyhydric alcohol (mol. wt. 180), if 2 g. are acetylated with acetyl chloride, and 36.1 ml. of 1.23 *N* NaOH are required to neutralize the liberated HCl? *Ans.* 4.

8. What would be the maximum normality of hydrobromic acid in the trap, if 100 g. of benzene are brominated with 140 g. of bromine (at. wt. 80), and the liberated HBr trapped in 200 ml. of water? *Ans.* 4.38 *N*.

9. What volume of 10 *N* HCl would be required to convert 17.3 g. of the color base of Malachite Green into its salt? *Ans.* 5 ml.

10. What is the *acid value* of a sample of Crisco if 6.3 ml. of 0.095 *N* KOH are required to neutralize a suspension of 2.7 g. of the fat in water? *Ans.* 12.4.

11. What volume of 0.152 *N* KOH would be required to neutralize a suspension in water of 4.5 g. of a fat whose *acid value* is 10.8? *Ans.* 5.65 ml.

12. What is the *saponification number* of a sample of Crisco if 27.5 ml. of 0.096 *N* KOH are required to neutralize the acid produced in the saponification of a 3.12-g. sample? *Ans.* 47.3.

13. What is the *saponification number* of Crisco which contains 22% stearin (mol. wt. 890), 68% olein (mol. wt. 884), and 10% linolein (mol. wt. 878)? *Ans.* 190.

14. What is the *Reichert-Meissl* number of a fat, if 13.4 ml. of 0.45 *N* KOH are required to neutralize the water-soluble, volatile fatty acids from the hydrolysis of 10.6 g. of fat? *Ans.* 28.4.

15. What are the *Reichert-Meissl* and the *Polenske* numbers of a sample of butter that contains 0.2% propionin, 3.2% butyrin, 1.4% caproin, 1.6% caprylin, 1.8% caprin, 6.9% laurin, 27.4% olein, 11.4% stearin, 22.6% myristin, and 22.6% palmitin? *Ans.* R-M = 17.1; P = 31.7.

16. If a sample of butter has a *Reichert-Meissl* number of 27, what volume of 0.1 *N*, and of 0.087 *N* KOH would be required to neutralize the water-soluble, volatile fatty acids from 6.0 g. of the butter? *Ans.* 32.5 ml.; 37.5 ml.

17. What volume of 0.15 *N* KOH would be required to neutralize the acid liberated in the saponification of a fat whose *saponification number* is 58? *Ans.* 16.5 ml.

18. What is the iodine number of linolein? *Ans.* 174.

19. What is the molecular weight of a glyceride that has an *iodine number* of 86.2, if it contains three double bonds? *Ans.* 884.

20. How many carbon-carbon double bonds does a glyceride contain, if it has a molecular weight of 872 and an *iodine number* of 262? *Ans.* 9.

21. What is the *iodine number* of linseed oil, if it contains 5% olein, 48.5% linolein, and 34.1% linolenin? *Ans.* 178.

A-5 MASS ACTION

A number of organic reactions are reversible and involve equilibria to which the usual laws of mass action apply. For a general reaction which may be represented by the equation,

$$aA + bB \rightleftharpoons cC + dD$$

where a moles of A react with b moles B to give c moles of C plus d moles of D, one can write an equilibrium equation of the form,

$$K = \frac{(C)^c \times (D)^d}{(A)^a \times (B)^b} \qquad (1)$$

Here, the letters in parentheses indicate the concentrations of C, D, A, and B, which are raised to the powers as indicated by corresponding superscripts. The concentrations will usually be expressed in moles per liter. The most common of the reversible reactions encountered are the dissociations of weak acids and bases and the hydrolyses of their salts.

Problem: What is the concentration of the hydrogen ion in 1 N acetic acid? The dissociation constant is 1.8×10^{-5}.

Solution: The equation for the dissociation or ionization of acetic acid is

$$\text{(a) } AcOH \rightleftharpoons AcO^- + H^+ \quad \text{or}^2 \quad \text{(b) } AcOH + H_2O \rightarrow AcO^- + H_3O^+$$

where AcOH represents the undissociated acetic acid, AcO^- the acetate ion, and H^+ the hydrogen ion. The equilibrium constant, i.e., dissociation or ionization constant, is then:

$$K_a = \frac{(AcO^-) \times (H^+)}{(AcOH)} = 1.8 \times 10^{-5} \qquad (2)$$

Since an equal number of acetate and hydrogen ions are produced by the ionization of the acetic acid, one can place them equal to each other. Also, the concentration of the undissociated acetic acid will be the initial concentration less the amount that ionizes. Thus, one can write

$$1.8 \times 10^{-5} = \frac{(H^+)(H^+)}{(1 - H^+)}$$

which is a quadratic equation with only one unknown. Simplification gives

$$(H^+)^2 + 1.8 \times 10^{-5}(H^+) - 1.8 \times 10^{-5} = 0$$

This can be solved by means of the quadratic formula:

$$x = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a}$$

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[2] Equations (a) and (b) are equivalent when water is the solvent, and only the more common one, (a), will be used.

where x is (H^+), b is 1.8×10^{-5}, a is 1, and c is 1.8×10^{-5}. Hence,

$$(H^+) = \frac{-1.8 \times 10^{-5} \pm \sqrt{3.24 \times 10^{-10} - 4 \times 1.8 \times 10^{-5}}}{2}$$

$$= \frac{-1.8 \times 10^{-5} \pm \sqrt{7.2 \times 10^{-5}}}{2}$$

$$= \frac{-1.8 \times 10^{-5} \pm 8.49 \times 10^{-3}}{2}$$

Obviously, one cannot use the negative sign, so that:

$$(H^+) = 4.25 \times 10^{-3}\, M$$

Thus, the concentration of hydrogen ion is $4.25 \times 10^{-3}\, M$, which is also the concentration of acetate ion. The concentration of unionized acetic acid is $1 - 0.00425 = 0.99575$. This is very close to 1, the molar concentration of the acetic acid. For this reason, a quicker approximate method may be used, as follows: Again placing the concentration of acetate ion equal to the concentration of hydrogen ion, which is always true if the only source of them is through dissociation, and assuming the concentration of the undissociated acetic acid is 1 M, one can substitute in equation (2) to obtain:

$$1.8 \times 10^{-5} = \frac{(H^+)^2}{1} \quad \text{or} \quad (H^+) = \sqrt{1.8 \times 10^{-5}}$$

Therefore, $(H^+) = 4.24 \times 10^{-3}\, M$. This method gives an answer which is sufficiently close to the accurate value when K_a is less than 10^{-3}.

In general, then, for the dissociation of an acid whose dissociation constant is not larger than 10^{-3} and whose concentration is C moles per liter, one can use the general formula:

$$K_a = \frac{(H^+)^2}{C}$$

which can be arranged to:

$$(H^+) = \sqrt{C \times K_a}$$

The same considerations apply to the dissociation of a weak base. The organic bases are the amines, which behave in solution similar to ammonia. Thus, for aqueous ammonia one writes

$$NH_3 + H_2O \rightleftharpoons [NH_4OH] \rightleftharpoons NH_4^+ + OH^-$$

and for an amine one may write

$$RNH_2 + H_2O \rightleftharpoons [RNH_3OH] \rightleftharpoons RNH_3^+ + OH^-$$

For the latter reaction one may write the equilibrium equation:

$$K_b = \frac{(RNH_3^+)(OH^-)}{(RNH_2)(H_2O)}$$

Since the solution will normally be dilute, the concentration of H_2O is affected very little by reaction with the amine. Its concentration remains practically the same and is therefore neglected. Again, if K_b is no larger than 10^{-3}, only a small amount of the amine will be in the ionic form and one can assume that its concentration is the total molarity of the amine. Also, (RNH_3^+) equals (OH^-), so that one may write:

$$K_b = \frac{(OH^-)^2}{C}$$

where C is the concentration of the amine. This can be rearranged to give $(OH^-) = \sqrt{K_b \times C}$.

Thus, for the dissociation of a weak acid whose concentration is C moles per liter, one has $(H^+) = \sqrt{K_a \times C}$; and for the dissociation of a weak base whose concentration is C moles per liter, one has $(OH^-) = \sqrt{K_b \times C}$.

Problem: What is the concentration of hydroxyl ion in an aqueous 0.5 N solution of ethyl amine? K_b for ethyl amine is 5.6×10^{-4}.

Solution: From the above equation:

$$\begin{aligned} (OH^-) &= \sqrt{K_b \times C} \\ &= \sqrt{5.6 \times 10^{-4} \times 0.5} \\ &= \sqrt{2.8 \times 10^{-4}} \\ &= 1.67 \times 10^{-2} \\ \text{Therefore, } (OH^-) &= 0.0167\ M \end{aligned}$$

Problem: What is the pH of a 1.5 M solution of sodium acetate?

Solution: Salts of weak acids or of weak bases hydrolyze in water and hence do not give neutral solutions.[3] The pH value is defined as the logarithm of the reciprocal of the hydrogen ion concentration. Mathematically, this is

$$pH = \log \frac{1}{(H^+)} = -\log (H^+)$$

Therefore, one must first determine the concentration of hydrogen ion to get the pH. The equation for the hydrolysis is

$$AcO^- + H_2O \rightleftharpoons AcOH + OH^-$$

The sodium ion is not included because the salt is completely ionized and the sodium-ion concentration is the same on both sides of the arrows. For this, one can write an equilibrium equation, again considering the concentration of H_2O to be constant:[4]

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[3] Salts from a weak acid plus a weak base will give a very nearly neutral solution because of the hydrolysis of both ions.

$$K_h = \frac{(AcOH)(OH^-)}{(AcO^-)} = \frac{K_w}{K_a} = \frac{10^{-14}}{K_a}$$

If K_h is not greater than 10^{-3}, and remembering that (AcOH) equals (OH^-), one can write

$$K_h = \frac{(OH^-)^2}{C} \quad \text{or} \quad (OH^-) = \sqrt{K_h \times C}$$

where C is the concentration of the salt in moles per liter. For sodium acetate:

$$K_h = \frac{10^{-14}}{1.8 \times 10^{-5}} = 5.56 \times 10^{-10}$$

Therefore, for the 1.5 M sodium acetate solution,

$$(OH^-) = \sqrt{1.5 \times 5.56 \times 10^{-10}} = \sqrt{8.34 \times 10^{-10}}$$

$$(OH^-) = 2.89 \times 10^{-5}\,M$$

If one knows either (H^+) or (OH^-), he can calculate the other from the relationship:

$$(H^+)(OH^-) = 10^{-14}$$

Consequently, here,

$$(H^+) = \frac{10^{-14}}{2.89 \times 10^{-5}} = 3.47 \times 10^{-10}\,M$$

The pH, then, is $\log \frac{1}{3.47} \times 10^{-10} = \log \frac{10^{10}}{3.47} = 10 - \log 3.47 = 10 - 0.54 = 9.46$.

By the same considerations, for a salt of a weak base one may write:

$$K_h = \frac{(H^+)^2}{C} \quad \text{or} \quad (H^+) = \sqrt{K_h \times C}$$

Here, $K_h = K_w/K_b$, where K_b is the dissociation constant of the weak base and K_w is the dissociation constant of water $= 10^{-14}$. By the simple rule, that salts of weak acids are basic and salts of weak bases are acidic, one can decide whether to solve for hydroxyl ion or hydrogen ion.

---

[4] For the dissociation of water,

$$H_2O \rightleftharpoons H^+ + OH^-$$

$$K = \frac{(H^+)(OH^-)}{(H_2O)}$$

If one lets the product K (H_2O) = K_w, it is found that

$$K_w = (H^+)(OH^-) = 10^{-14}$$

Upon dividing the ion product of water, $(H^+)(OH^-) = K_w$, by the dissociation equation for acetic acid $\frac{(AcO^-)(H^+)}{(AcOH)} = K_a$, the above equation for hydrolysis results. This is equal to $\frac{K_w}{K_a}$

In general, then, there are four cases which produce acidic or basic solutions, and for each case there is a simple equation by which one may calculate the hydrogen or hydroxyl ion concentration:

$(H^+) = \sqrt{K_a \times C}$ dissociation of a weak acid

$(OH^-) = \sqrt{K_b \times C}$ dissociation of a weak base

$(H^+) = \sqrt{K_h \times C}$ hydrolysis of the salt of a weak base $(K_h = K_w/K_b)$

$(OH^-) = \sqrt{K_h \times C}$ hydrolysis of the salt of a weak acid $(K_h = K_w/K_a)$

Problem: Calculate the degree of dissociation of a 0.2 *M* solution of isobutylamine. $K_b = 3.1 \times 10^{-4}$.

Solution: The degree of dissociation of an acid or base is the amount that dissociates divided by the initial amount, times 100 to give a percentage. Thus, one must know how much of the isobutylamine hydroxide has dissociated, i.e., the concentration of hydroxide ion.

From the equation $(OH^-) = \sqrt{K_b \times C}$, one may write:

$$\begin{aligned}(OH^-) &= \sqrt{0.2 \times 3.1 \times 10^{-4}}\\ &= \sqrt{62 \times 10^{-6}}\\ &= 7.87 \times 10^{-3}\,M\end{aligned}$$

Therefore, the degree of dissociation is

$$\frac{0.00787}{0.2} \times 100 = 3.94\%$$

Problem: Calculate the concentration of hydrogen ion in a solution of 10 g. of propionic acid in 200 ml. of water to which 0.5 g. of sodium propionate has been added. $K_a = 1.33 \times 10^{-5}$.

Solution: The approximate equations above cannot be used because this is not a simple dissociation or hydrolysis. The one relationship that holds is:

$$K_a = \frac{(\text{propionate ion})(H^+)}{(\text{propionic acid})}$$

Propionate ion is produced by dissociation of the propionic acid and from the sodium propionate, as are the other substances in this equation produced from two sources. The concentration of sodium propionate is

$$0.5/96 \times (1000/200) = 0.0261\,M$$

and that of the propionic acid is

$$10/74 \times (1000/200) = 0.595\,M$$

It was shown above that the hydrolysis of the salt and dissociation of the acid is quite small; thus the actual concentration of propionate ion is very close to the concentration of sodium propionate, and the concentration of undissociated propionic acid is very close to its total molarity. Therefore, as a first approximation one may write

$$K_a = \frac{(0.0261)(H^+)}{0.595} = 1.33 \times 10^{-5}$$

$$(H^+) = \frac{1.33 \times 10^{-5} \times 0.595}{0.0261}$$

$$= 3.04 \times 10^{-4}\,M$$

Problem: What is the concentration of hydroxide ion in 250 ml. of a 1 *M* solution of methylamine ($K_b = 6.4 \times 10^{-4}$) to which has been added 0.2 g. of methylamine hydrochloride?

Solution: The equation for the ionization is $CH_3NH_2 + H_2O = CH_3NH_3OH = CH_3NH_3^+ + OH^-$, for which one may write an equilibrium equation of the form:

$$K_b = \frac{(CH_3NH_3^+)(OH^-)}{(CH_3NH_3OH)} = 6.4 \times 10^{-4}$$

As above, one can assume that the concentration of $CH_3NH_3^+$ is the same as that of the salt, and that the concentration of the free base is 1 *M*. The concentration of CH_3NH_3Cl is $\frac{0.2}{65}$ (1000/250) = 0.012 *M*; therefore one has

$$\frac{(0.012)(OH^-)}{1} = 6.4 \times 10^{-4}$$

$$(OH^-) = \frac{6.4 \times 10^{-4}}{0.012} = 5.33 \times 10^{-2}\,M$$

Problem: What is the concentration of hydrogen ion and the degree of hydrolysis in a solution containing 15 g. per liter of dimethylamine hydrochloride? K_b for dimethylamine is 4.9×10^{-4} *M*.

Solution: The salt of an amine may be treated just as ammonium chloride. It was shown in general chemistry that ammonium chloride is completely ionized in water solution and that due to hydrolysis of the ammonium ion, the solution is mildly acidic. This also applies to amine salts.

Thus,

$$NH_4Cl \rightarrow NH_4^+ + Cl^-$$

$$NH_4^+ + H_2O \rightleftarrows NH_4OH + H^+$$

$$K_h = \frac{(NH_4OH)(H^+)}{(NH_4^+)} = \frac{(H^+)^2}{(C-H^+)} = \frac{K_w}{K_b}$$

and for an amine salt,

$$RNH_3Cl \rightarrow RNH_3^+ + Cl^-$$

$$RNH_3^+ + H_2O \rightleftarrows RNH_3OH + H^+$$

$$K_h = \frac{(RNH_3OH)(H^+)}{(RNH_3^+)} = \frac{(H^+}{(C-H^+)} = \frac{K_w}{K_b}$$

Therefore, for this problem:

$$K_h = \frac{10^{-14}}{4.9 \times 10^{-4}} = 2.04 \times 10^{-11}$$

$$C = \frac{15}{81.5} = 0.184\ M$$

Therefore,

$$H^+ = \sqrt{C \times K_h} = \sqrt{0.184 \times 2.04 \times 10^{-11}}$$

$$= \sqrt{3.76 \times 10^{-12}}$$

$$= 1.94 \times 10^{-6}\ M$$

The degree of hydrolysis (X) is the fraction of the salt which is hydrolyzed.

$$X = \frac{(RNH_3OH)}{C} = \frac{(H^+)}{C}$$

$$= \frac{1.94 \times 10^{-6}}{184} = 1.05 \times 10^{-4}$$

Problem: Calculate the pH necessary to insure at least 99% conversion of a 0.5 M solution of toluidine ($K_b = 3.3 \times 10^{-10}$) to toluidine hydrochloride.

Solution: In the process of neutralization, the equilibrium involving the undissociated base, the anion of the salt and the components of water is maintained according to the equation:

$$K_b = \frac{(CH_3C_6H_4NH_3^+)(OH^-)}{(CH_3C_6H_4NH_3OH)} = 3.3 \times 10^{-10}$$

One can assume that the concentration of $CH_3C_6H_4NH_3^+$ is the same as that of the salt produced. A 99% conversion of the amine to its salt would result in a $(0.99 \times 0.5) = 0.495\ M$ salt solution. The concentration of free base is, then,

$$0.5 - 0.495 = 0.005\ M$$

Therefore, one has

$$\frac{(0.495)(OH^-)}{5 \times 10^{-3}} = 3.33 \times 10^{-10}$$

$$(OH^-) = \frac{1.65 \times 10^{-12}}{0.495} = 3.33 \times 10^{-12}$$

$$(H^+) = \frac{10^{-14}}{3.33 \times 10^{-12}} = 3 \times 10^{-3}$$

$$pH = -\log (H^+) = -\log (3 \times 10^{-3})$$

$$pH = 3 - \log 3 = 3 - 0.477$$

$$\therefore pH = 2.52$$

Problem: In the preparation of trimethyl ammonium chloride, 2.36 g. of trimethylamine was collected in 100 ml. of water. When the amine was converted to its salt with hydrochloric acid, what pH was necessary to insure 90% conversion?

Solution: The concentration of the amine is first expressed in moles per liter.

$$\text{wt. per 1000 ml:}\quad \frac{2.36}{100} = \frac{\text{wt.}}{1000}, \qquad \text{wt.} = 23.6\ \text{g}$$

$$\frac{23.6}{59} = 0.4 \text{ mole per liter}$$

$$K_b = \frac{((CH_3)_3NH^+)(OH^-)}{((CH_3)_3NHOH)} = 5.27 \times 10^{-5}$$

As in the previous problem, one can assume that the concentration of the ion (in this case, $(CH_3)_3NH^+$) equals that of the salt. The concentration of the salt is $0.4 \times 0.90 = 0.36\ M$. The concentration of free base is then, $0.4 - 0.36 = 0.04\ M$. Therefore,

$$\frac{0.36\,(OH^-)}{0.04} = 5.27 \times 10^{-5}$$

$$(OH^-) = \frac{2.1 \times 10^{-6}}{0.36} = 5.83 \times 10^{-6}$$

$$(H^+) = \frac{10^{-14}}{5.83 \times 10^{-6}} = 1.71 \times 10^{-9}$$

$$pH = -\log (H^+) = -\log (1.71 \times 10^{-9})$$

$$pH = 9 - \log 1.71 = 9 - 0.233 = 8.77$$

A more general solution is as follows: The equilibrium constant for ionization of a weak acid can be expressed in terms of pH and pK_a:

$$HA \rightleftharpoons H^+ + A^-$$

$$K_a = \frac{(H^+)(A^-)}{(HA)} \quad \text{or} \quad H^+ = K_a \cdot \frac{(HA)}{(A^-)}$$

Taking logs of both sides and by definition of pH,

$$pH = pK_a - \log \frac{(HA)}{(A^-)}$$

For $(CH_3)_3N$, $K_b = 5.27 \times 10^{-5}$, $pK_b = 4.28$, $pK_a = 9.72$. In this problem, the ratio of $HA/A^- = (CH_3)_3N^+H/(CH_3)_3N = 9:1$

$$pH = 9.72 - \log 9/1$$

$$= 9.72 - 0.95 = 8.77$$

Problem: What pH is necessary to liberate butyric acid from a 0.5 *M* solution of sodium butyrate? K_a for butyric acid is 1.506×10^{-5}.

Solution: Again, the undissociated acid, its ion, and the components of water are in equilibrium according to the equation:

$$K_a = \frac{(C_3H_7COO^-)(H^+)}{(C_3H_7COOH)} = 1.506 \times 10^{-5}$$

The condition sought is that when butyric acid alone is dissolved in water. Hence, the concentration of the butyrate ion and hydrogen ion are equal and the concentration of undissociated butyric acid is close to the molar concentration of organic acid. Here, it would be 0.5 *M*. Therefore, one has

$$\frac{(H^+)^2}{0.5} = 1.506 \times 10^{-5}$$

$$(H^+)^2 = 1.506 \times 10^{-5} \times 0.5$$

$$= 7.53 \times 10^{-6}$$

$$(H^+) = 2.74 \times 10^{-3}$$

$$\log (H^+) = 3.438$$

$$\therefore pH = 2.56$$

Of course, the practical thing to do would be to make the solution even more acidic, in order to convert as much as possible of the small equilibrium amount of salt to the acid.

Problem: What is the pH of a solution that could be used to separate 2,4-dinitro-o-cresol ($K_a = 4.5 \times 10^{-5}$) from phenol ($K_a = 1.3 \times 10^{-10}$) by extraction?

Solution: On the assumption that these two phenols are only negligibly soluble in water and that their salts are soluble, their separation is brought about by converting as much as possible of the stronger acid to its salt without appreciable neutralization of the weaker acid. If the two acids are dissolved in ether and shaken with a buffered aqueous solution, then the aqueous phase should be at a pH midway between the pK_a values of the acids. The pK_a's are 4.35 and 9.89 for the nitrophenol and phenol, respectively. Thus, at a pH of 7.12,

Nitrophenol

$$7.12 = 4.35 - \log \frac{(HA)}{(A^-)}$$

$$-2.77 = \log \frac{(HA)}{(A^-)}$$

$$\frac{(A^-)}{(HA)} = 600$$

Phenol

$$7.12 = 9.89 - \log \frac{(HA)}{(A^-)}$$

$$\frac{(A^-)}{(HA)} = 1.7 \times 10^{-3}$$

That is, even if the acid forms were soluble in water, at $pH = 7.12$, the ratio of salt to acid form would be 600 for the nitrophenol and about 1/1000th for the phenol. Since the acid is not very soluble, the concentration of salt of the phenol is negligible.

Problem: Can phenol, $K_a = 1.3 \times 10^{-10}$, be extracted from an ether solution with excess 10% aqueous sodium carbonate? K_2 for carbonic acid is 5.5×10^{-11}.

Solution: We will first find the pH of a solution of sodium phenoxide and also of the sodium carbonate and see if the pH of the latter solution is high enough to retain the sodium phenoxide.

For sodium phenoxide,

$$K_h = \frac{10^{-14}}{1.3 \times 10^{-10}}$$

$$= 7.7 \times 10^{-5}$$

$$(OH^-) = \sqrt{7.7 \times 10^{-5} \times 2} = 1.24 \times 10^{-2}\,M$$

$$(H^+) = \frac{10^{-14}}{1.24 \times 10^{-2}} = 8.04 \times 10^{-13}$$

$$\log (H^+) = \overline{13}.905$$

$$\therefore pH = 12.1$$

Sodium carbonate hydrolyzes to sodium bicarbonate, and its pH is calculated as follows:

$$K_h = \frac{K_w}{K_a} = \frac{10^{-14}}{5.5 \times 10^{-11}} = 1.785 \times 10^{-4}.$$

$$(OH^-) = \sqrt{1.785 \times 10^{-4} \times 1} \quad 1.33 \times 10^{-2}$$

$$(H^+) = \frac{10^{-14}}{1.33 \times 10^{-2}} = 7.5 \times 10^{-13}$$

$$\log (H^+) = \overline{13}.875$$

$$pH = 12.1$$

Thus, the sodium carbonate solution has just the basicity that sodium phenoxide has, and hence the phenol will dissolve in the carbonate solution. However, an excess of the solvent must be used so that the pH will be little affected when the phenol neutralizes some of the sodium carbonate.

EXERCISES

1. What is the concentration of hydrogen ion in a 0.2 N solution of phenylacetic acid? $K_a = 4.88 \times 10^{-5}$. *Ans.* 3.13×10^{-3}.

2. What is the concentration of hydroxide ion in 200 ml. of an aqueous solution containing 5 g of isoamylamine? $K_b = 5 \times 10^{-4}$. *Ans.* 0.012 M.

3. What is the concentration of hydrogen ion in a solution containing 15 g per liter of propylamine hydrochloride? K_b for propylamine is 4.7×10^{-4}. *Ans.* 1.83×10^{-6}.

4. What is the degree of hydrolysis of a 1 M solution of aniline hydrochloride? K_b for aniline is 5.4×10^{-10}. *Ans.* 0.431%.

5. What is the degree of hydrolysis of a 0.2 M solution of sodium valerate? K_a for valeric acid is 1.38×10^{-5}. *Ans.* 6×10^{-3}%.

6. What is the concentration of hydrogen ion in a solution containing 50 g. of butyric acid and 2 g. of sodium butyrate per 450 ml.? K_a for butyric acid is 1.5×10^{-5}.
Ans. 4.69×10^{-4} *M*.

7. What *p*H is necessary to insure at least 99% conversion of a 0.6 *M* solution of dimethylamine to its salt with hydrochloric acid? K_b for dimethylamine is 4.9×10^{-4}.
Ans. 8.7.

8. What maximum *p*H would be used to liberate propionic acid from a solution of 0.4 *M* potassium propionate? K_a for propionic acid is 1.343×10^{-5}. *Ans.* 2.64.

9. Can 5% sodium bicarbonate (~0.5 *M*) be used to dissolve most carboxylic acids ($K_a \simeq 10^{-5}$)? K_a for carbonic acid is 4.3×10^{-7}.
Ans. Yes (the margin is so close that a large excess of sodium bicarbonate solution is required).

10. What is the *p*H of a solution which can be used for the removal of di-isoamylamine ($K_b = 7.7 \times 10^{-4}$) from an ether solution of a mixture of di-isoamylamine and benzidine ($K_b = 9.3 \times 10^{-10}$)?
Ans. 5.2.

11. Pyridine ($K_b = 1.4 \times 10^{-9}$) and ethanolamine ($K_b = 2.77 \times 10^{-5}$) are both very soluble in water. At what *p*H should a 2 *M* aqueous solution of a mixture of these two be extracted with chloroform by continuous extraction to effect their separation (i.e., remove the pyridine)? *Ans.* 4.6.

Another type of common organic equilibrium reaction is esterification. The general equation is

$$\mathrm{RCOOH + R'OH \overset{H^+}{\rightleftharpoons} RCOOR' + H_2O}$$

Hydrogen ion is the catalyst here, but a catalyst does not influence the position of equilibrium but rather, the rate at which equilibrium is reached. In this reaction, the concentration of water is not the same on both sides of the arrows and cannot be neglected. One may write an equilibrium equation as:

$$\mathrm{K = \frac{(RCOOR')(H_2O)}{(RCOOH)(R'OH)}}$$

where the formulas in parentheses represent the respective concentrations in moles per liter.

Problem: Calculate the percentage conversion of 2 moles of acetic acid when it is allowed to come to equilibrium with 6 moles of ethyl alcohol. At 25° the equilibrium constant is found to be 4.

Solution: Assume that at equilibrium, *X* moles of acetic acid have reacted with *X* moles of alcohol, and that the total volume of liquid is *V* liters. The concentrations in moles per liter of the components of this equilibrium at the start of the reaction, and when equilibrium is reached, are:

	Acid	*Alcohol*	*Water*	*Ester*
At start:	$2/V$	$6/V$	$0/V$	$0/V$
At equil:	$\frac{2-X}{V}$	$\frac{6-X}{V}$	X/V	X/V

The equilibrium equation is then:

$$K \quad \frac{\frac{X}{V} \cdot \frac{X}{V}}{\frac{(2-X)}{V}\frac{(6-X)}{V}} = 4$$

Since V occurs throughout, it can be canceled, and one has

$$4 = \frac{X^2}{(2-X)(6-X)}$$

Simplification and rearrangement gives:

$$4(2-X)(6-X) = X^2$$
$$4(12-8X+X^2) = X^2$$
$$3X^2 - 32X + 48 = 0$$

By means of the quadratic formula one gets:

$$X = \frac{32 \pm \sqrt{32^2 - 4 \times 3 \times 48}}{2 \times 3}$$
$$= \frac{32 \pm \sqrt{1024 - 576}}{6}$$
$$= \frac{32 \pm 21.2}{6}$$

The positive sign would give an impossible answer; thus, one has

$$\frac{10.8}{6} = 1.8$$

That is, 1.8 moles of ethyl acetate are formed, and the per cent conversion is

$$\frac{1.8}{2} \times 100 = 90\%$$

EXERCISES

1. Calculate the percentage conversion of 1.5 moles of acetic acid when allowed to come to equilibrium with 5 moles of ethyl alcohol. *Ans.* 91.1%.

2. What weight of alcohol and ester will there be at equilibrium[5] at 25° in a mixture of 20 g. of ethyl acetate and 30 g. of water?

Ans. 7.4 g. of ethyl alcohol and 5.9 g. ethyl acetate.

---

[5] Given the equation for a reaction,

$$A + B \rightleftharpoons C + D$$

the equilibrium constant K can be expressed

$$K = \frac{(C)(D)}{(A)(B)}$$

If the equation is written in the reverse direction, $C + D \rightleftharpoons A + B$, the new equilibrium constant K′ is the reciprocal of the former, i.e.,

$$K' = \frac{(A) \times (B)}{(C) \times (D)} = \frac{1}{K}.$$

3. A mixture of 0.3 mole of pure ethyl alcohol and 0.1 mole of pure butyric acid was allowed to stand until equilibrium was established. The mixture was then titrated with a base so rapidly that no ethyl butyrate hydrolysed. To neutralize the solution, 150 ml. of 0.5 N alkali were required. Find the value of the equilibrium constant.
Ans. K = 0.0303.

A-6 LABORATORY OPERATIONS

a. Extraction. When a solution of a substance in one solvent is shaken with a second solvent which is immiscible with the first, the solute distributes itself between the two solvents in such a way that a definite ratio is set up between the concentrations of the solute in the two phases. The equilibrium is represented by the equation, $C_1/C_2 = \mathrm{K}$, where C_1 and C_2 are the concentrations of the solute in the two solvents, and K, usually called the partition coefficient, is a constant.

Problem: A substance is five times as soluble in ether as in water. An aqueous solution of the substance contains 15 g. per 100 ml. of solution. If 100 ml. of this solution is shaken with 50 ml. of ether, what weight of the substance will be found in the ether layer?

Solution: Let X be the amount that goes into the ether, then $15 - X$ is the amount that remains in the water; $X/50$ is the concentration in the ether and $\dfrac{15 - X}{100}$ is the concentration in the water.

Then:

$$\frac{\dfrac{X}{50}}{\dfrac{15 - X}{100}} = 5$$

$$\frac{X}{50} = \frac{5\,(15 - X)}{100} = \frac{75 - 5X}{100}$$

$$\frac{100X}{50} = 75 - 5X$$

$$2X = 75 - 5X$$

$$7X = 75$$

$$X = 10.7 \text{ g.}$$

Thus, 10.7 g. are in the ether layer and 15 − 10.7 = 4.3 g. remain in the water layer.

This can be generalized for any pair of immiscible solvents. If a solution, containing a grams of solute in v_1 ml. of solvent A, is shaken with v_2 ml. of solvent B, then the amount of solute that will be found in solvent B and A will be X and $a - X$, respectively. That is,

$$\frac{\dfrac{X}{v_2}}{\dfrac{a - X}{v_1}} = \mathrm{K}$$

Problem: Suppose the water solution above were shaken with two 25-ml. portions instead of one 50-ml. portion of ether, what weight of the solute would then be removed from the water solution?

Solution: Here, $X/25$ is the concentration of the solute in ether and $\frac{15 - X}{100}$ the concentration of the solute in the H_2O layer. Thus,

$$\frac{\frac{X}{25}}{\frac{15 - X}{100}} = 5$$

$$\frac{X}{25} = \frac{5(15 - X)}{100}$$

$$\frac{100X}{25} = 75 - 5X$$

$$4X = 75 - 5X$$

$$X = 8.33 \text{ g.}$$

The weight of the solute remaining in water solution is 15 − 8.33 = 6.67 g. For the second shaking, $X'/25$ is the concentration of the solute in ether and $\frac{6.67 - X'}{100}$ is the concentration in H_2O.

$$\frac{\frac{X'}{25}}{\frac{6.67 - X'}{100}} = 5$$

Hence,

$$\frac{100X'}{25} = 5(6.67 - X')$$

$$4X' = 33.35 - 5X'$$

$$X' = 3.71 \text{ g.}$$

Therefore, the total weight of solute that has been removed is 8.33 + 3.71 g. = 12.04 g., while 15 − 12.04 = 2.96 g. remained dissolved in the water. If this is compared with the amount left after one 50-ml extraction, it is seen that 4.3 − 2.96 = 1.34 g. (or about 9%) more of the solute was removed after the two 25-ml. extractions.

EXERCISES

1. When 5 g. of aniline was shaken with a mixture of 100 ml. of water and 50 ml. of ether, the ether layer was found to contain 4.17 g. of aniline and the water layer 0.83 g. of aniline. Calculate the partition coefficient of aniline between ether and water. *Ans.* 10.

2. One liter of water containing 14 g. of aniline was extracted with two successive 100-ml. portions of ether. What weight of aniline remained in the water layer after the second extraction? *Ans.* 3.5 g.

b. Steam distillation. When two or more mutually immiscible substances are mixed, the vapor pressure of each substance is independent of the other and the vapor pressure of each substance is what it would be if it were alone. The total vapor pressure at any given temperature is the sum of the individual partial pressures at that temperature. The number of moles of each substance in the vapor state will, of course, be proportional to the respective vapor pressure. This is expressed for two substances by the relationship:

$$\frac{n_a}{n_b} = \frac{p_a}{p_b}$$

where n and p are the number of moles and the partial pressure, respectively. Since the distillate is approximately of the same concentration as the vapor above the boiling liquid, this indicates the relative amounts of two immiscible liquids that will co-distill. Two immiscible liquids will co-distill when the sum of their partial pressures is equal to the atmospheric pressure.

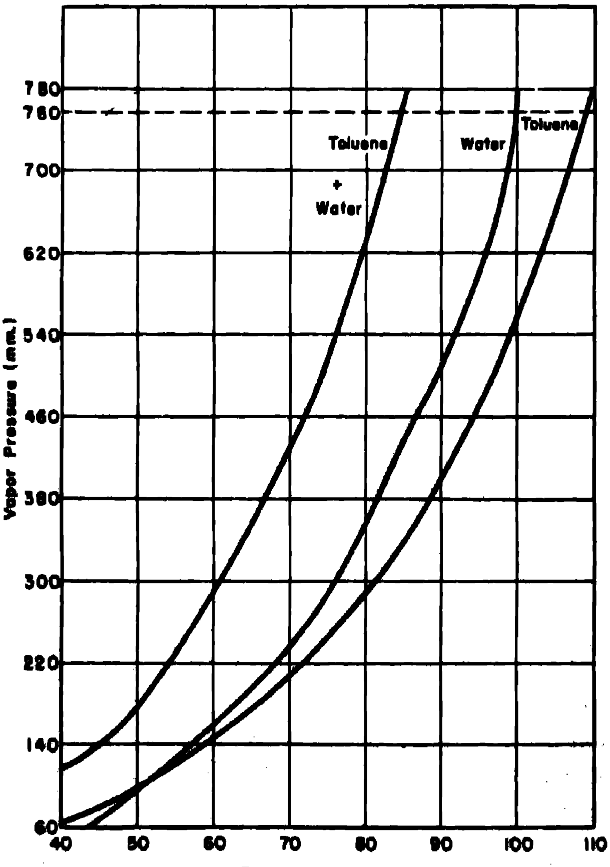

Fig. A.1. Vapor pressure-temperature graph for toluene, water, and toluene plus water.

The boiling point and the vapor pressure at the boiling point of a mixture of two immiscible liquids can be found by determining at what temperature the sum of the two vapor pressures is equal to atmospheric pressure. This is easily done by plotting vapor pressure versus temperature for each component, and then adding the vapor pressures at various temperatures and plotting these sums against temperature. The temperature at which this curve of total vapor pressure crosses the atmospheric pressure line is the boiling point of this mixture. Then, at this temperature the separate vapor pressures may be read from the individual curves. For illustration, see Figure A.1 for toluene and water. The toluene + water curve is observed to cross the 760-mm. line at about 84.5°. From the toluene curve, it is found that the vapor pressure of toluene at this temperature is 336 mm., and from the water curve, the vapor pressure of water at 84.5° is found to be 424 mm.

Problem: At 66.5° the vapor pressures of water and CCl_4 are 200 mm. and 560 mm., respectively. What weight of CCl_4 will be found in the distillate after 1 l. of water has been collected?

Solution: Using the equation

$$\frac{n_{CCl_4}}{n_{H_2O}} = \frac{P_{CCl_4}}{P_{H_2O}}$$

where $P_{CCl_4} = 560$, $P_{H_2O} = 200$, and $n_{H_2O} = 1000/18 = 55.6$ (assuming the density of water to be 1 g./ml.). After substitution in the equation, one gets

$$n_{CCl_4} = 55.6 \times \frac{560}{200} = 155.8, \text{ or } 156 \text{ moles}$$

Therefore, weight $CCl_4 = 156 \times 154 = 24{,}000$ g.

EXERCISES

1. At what temperature will a mixture of aniline and water steam distill and what weight of aniline will distill per liter of water? *Ans.* 98.5°; 287 g.

2. At 97°, the vapor pressures of *o*-chlorobromobenzene and water are 95 mm. and 665 mm., respectively. What minimum quantity of water would be required to steam distill 100 g. of *o*-chlorobromobenzene? *Ans.* 65.7 ml.

c. Fractional distillation. If two liquids form a solution which is almost ideal, or if one assumes that the solution obeys Raoult's law, then one may calculate the composition of any mixture of the two liquids that boils at a given temperature below the boiling point of the higher boiling liquid. Also, the composition of the vapor in equilibrium with the boiling liquid may be determined, which, in absence of refluxing, represents the composition of the first part of the distillate.

Problem: The vapor pressures of pure nitrobenzene and of pure benzene at 100° are 20.8 and 1340 mm., respectively. What is the composition of a mixture of the two which boils at 100° at 760 mm. pressure? What would be the weight per cent of nitrobenzene in the first portion of the distillate?

Solution: Assuming Raoult's law to hold, one has:

$$P_b = P_{o_b} N_b \tag{1}$$

$$P_n = P_{o_n} N_n \tag{2}$$

where P_b and P_n are the partial vapor pressures of benzene and nitrobenzene, P_{o_b} and P_{o_n} are the vapor pressures of the pure separate components at the same temperature, and N_b and N_n are the mole fractions of the two components in the solution. Also:

$$N_b + N_n = 1 \tag{3}$$

$$P_b + P_n = 760 \tag{4}$$

Solve (1) and (2) simultaneously with the aid of (3) and (4). From (3), $N_b = 1 - N_n$, and from (4), $P_b = 760 - P_n$, which can be substituted in (1) for P_b and N_b. This gives the equation:

$$760 - P_n = P_{o_b}(1 - N_n)$$

Now, use the numerical value of 1340 for P_{o_b}, and from (2) substitute the value $P_{o_n}N_n$ for P_n to give

$$760 - (P_{o_n}N_n) = 1340(1 - N_n)$$

By using the numerical value of P_{o_n}, one gets an equation with one unknown, N_n:

$$760 - 20.8N_n = 1340(1 - N_n)$$

Simplification gives

$$1319N_n = 580$$

Therefore,

$$N_n = 580/1319 = 0.44 \text{ or } 44\%$$

$$N_b = 1 - 0.44 = 0.56 \text{ or } 56\%$$

These are mole per cents. The ratio of the weight of nitrobenzene to the weight of benzene is

$$\frac{\text{Wt. nitrobenzene}}{\text{Wt. benzene}} = \frac{44 \times 123}{56 \times 78} = \frac{5410}{4370} = 1.24$$

and the weight per cent of nitrobenzene in solution is

$$\frac{5410}{5410 + 4370} \times 100 = 55.3\%$$

Hence, the per cent by weight of the benzene is 44.7, which means that the composition of the solution is 55.3% nitrobenzene and 44.7% benzene by weight.

Now, to get the composition of the first portion of the distillate, calculate the partial pressures of the initial vapor in equilibrium with the boiling solution. From equations (1) and (2),

$$P_b = P_{o_b}N_b$$

$$= 1340 \times 0.56 = 751 \text{ mm.}$$

and

$$P_n = P_{o_n}N_n$$

$$= 20.8 \times 0.44 = 9.15 \text{ mm.}$$

The total, of course, should equal 760 mm. In the vapor phase the mole fractions of the components are:

$$N_b = \frac{P_b}{P_n + P_b} \quad \text{and} \quad N_n = \frac{P_n}{P_b + P_n}$$

Therefore,

$$N_b = \frac{751}{760} = 0.988 \text{ or } 98.8\%$$

$$N_n = \frac{9}{760} = 1.2\%$$

The ratio of weight is

$$\frac{\text{Wt. benzene}}{\text{Wt. nitrobenzene}} = \frac{98.8 \times 78}{1.2 \times 123} = \frac{771}{148}$$

and the weight per cent of benzene is

$$\frac{771}{771 + 148} = 84\%$$

The weight per cent of nitrobenzene is thus 16%. This indicates that a solution of 44.7% benzene in nitrobenzene produces an 84% benzene solution when it first begins to distill.

EXERCISES

1. At 66.5°C. the vapor pressure of pure $CHCl_3$ (mol. wt. 120) is 920 mm. and that of CCl_4 (mol. wt. 154) is 560 mm. Assuming Raoult's law to hold, calculate the mole fractions of $CHCl_3$ and CCl_4 in a mixture of the two which boils at 66.5° under 760 mm. pressure. *Ans.* $N_{CHCl_3} = 0.555$; $N_{CCl_4} = 0.445$.

2. What is the composition by weight of the first vapors given off when the above mixture boils? *Ans.* 61.2% $CHCl_3$; 38.7% CCl_4.

d. Distillation at reduced pressures.[6] The vapor pressure of a liquid is given by the equation:

$$\ln p = -\frac{\Delta H}{RT} + I \tag{1}$$

or in logs to the base 10,

$$4.578 \log p = -\frac{\Delta H}{T} + I$$

where ΔH is the heat of vaporization in calories, T is the absolute temperature of the boiling point, p is the vapor pressure in atmospheres, and I is Trouton's constant. Over short temperature ranges, the vapor pressure of many liquids is given by the equation:

$$\log p = \frac{-0.05223a}{T'} + b$$

The empirically determined constants a and b are listed in most handbooks for a number of substances. If they are not available, and if only the boiling point of the compound at atmospheric pressure is known, an estimate of the boiling point at reduced pressures may be made within satisfactory limits.

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[6] An excellent discussion of the graphic estimation of boiling points at reduced pressures has been given by G. R. Robertson, *J. Chem. Educ.* **27**, 341 (1950).

From Equation 1, one can see that when the pressure is 1 atmosphere, $I = \Delta H/T$, which is Trouton's rule. The value of Trouton's constant,[7] I, runs from about 20 for nonpolar compounds, such as ethers, hydrocarbons, etc., to 27 for associated liquids, such as alcohols and acids (page 162). It would be within experimental error to use 26 for water, alcohols, and acids, and 21 for all other compounds.

Problem: What is the boiling point of propanol at 300 mm. pressure? Its boiling point at 760 mm. is 97°.

Solution: Using 26 as Trouton's constant, one has:

$$\Delta H = 26 \times (97 + 273)$$
$$\simeq 9610$$

Hence,

$$4.578 \log (300/760) = -\frac{9610}{T} + 26$$

$$4.578(-0.4037) = \frac{-9610}{T} + 26$$

$$T = 9610/32.43 = 345°\text{K}.$$
$$= 72°\text{C}. \text{ (observed b.p. at 301 mm. is 75°)}$$

Conversely, by equation (1) one could calculate the vapor pressure of a substance at a given temperature. The same technique would be used, except T would be known and one would solve for p.

Sometimes, only the boiling point at reduced pressure is known, and the boiling point at some other reduced pressure is desired. In that case, a different form of equation 1 may be used, such as:

$$\log \frac{P_2}{P_1} = \frac{\Delta H(T_2 - T_1)}{2.303 \times 1.987 \times T_2 T_1}$$

where P_2 and P_1 are the vapor pressures at temperatures T_2 and T_1, respectively, and ΔH is the heat of vaporization.

Problem: The boiling point of a certain aldehyde at 50 mm. is 135°. What is its approximate boiling point at 12 mm.?

Solution: Here, a less accurate estimate of the heat of vaporization must be made. Usually substances that are distilled at reduced pressures are those whose normal boiling points are above 200°. If one takes 250° as an average boiling point, then the heats of vaporization will range from about 20 × (250 + 273) = 10,460 cal. for nonpolar liquids, to 26 × (523) = 13,600 cal. for polar liquids. A reasonable average value to take as the heat of vaporization of these high-boiling liquids is 12,000 cal. Estimates made on this basis will have a 5° to 10° deviation from the experimental value. The boiling point varies greatly with experimental conditions; therefore, for the characterization of liquids, properties are chosen such as the index of refraction and the density. Primarily, what is desired here is an approximation of the boiling range.

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[7] See the Table compiled by Robertson, *ibid.*

If one assumes the heat of vaporization of the aldehyde to be 12,000 cal., upon substitution in equation 2 one gets:

$$\log (12/50) = \frac{12{,}000(T_2 - 408)}{4.578 \times 408T_2}$$

$$-0.62 \times 4.578 \times 408T_2 = 12{,}000T_2 - 4.9 \times 10^6$$

$$T_2 = \frac{4.9 \times 10^6}{1.316 \times 10^4}$$

$$= 373°\text{K}.$$

$$\therefore T_2 = 100°\text{C}.$$

EXERCISES

1. The boiling point of ethyl *n*-butylacetoacetate at 12 mm. is found to be 104°. What would be its boiling point at 760 mm.?

Ans. 236° (assuming $\Delta H = 12{,}000$ cal.)

2. The boiling point of ethyl furoylacetate is found to be 170° at 20 mm. Calculate its boiling point at 10 mm. Compare this with 143°, the observed boiling point at this pressure. *Ans.* 149°

$$\frac{149° - 143°}{143} \times 100 = 4.2\% \text{ (error)}.$$

3. The boiling point of *n*-tetradecane is 253° at 760 mm. Calculate its boiling point at 10 mm. pressure. *Ans.* 109°.

A-7 OXIDATION-REDUCTION REACTIONS

Half-reaction method. As stated in Section 6.7, methods of balancing equations for redox reactions are quite arbitrary and most teachers have their own preferential techniques for doing this. The same principles are involved in balancing equations for organic as for inorganic reactions, although the determination of the relative oxidation stage of elements in organic compounds is usually less exact.[8] The procedure recommended in Section 6.7 involves the half-reaction method, and consists of the following steps for balancing each half-reaction.[9]

Step 1: Balance all elements except hydrogen and oxygen.

Step 2: Bring oxygen to a balance with H_2O molecules; then bring hydrogen to a balance with protons.

Step 3: Balance ionic charges with electrons.

Step 4: (for alkaline media): Remove excess protons by adding an equal number of hydroxide ions to both sides of the arrow.

Before working examples, several points should be brought forward. Potassium dichromate and potassium permanganate are the most common oxidizing agents used in organic chemistry and it is to be known that their reduction products in aqueous solution are as follows, where the substances are written in their ionic forms:

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[8] L. N. Ferguson has described a method of determining relative oxidation stages of elements in organic compounds in the *J. Chem. Educ.* **23**, 550 (1946).

[9] The author is indebted to Dr. Gus Dorough for this procedure.

Acid Media	*Alkaline or Neutral Media*
$Cr_2O_7^{=} \rightarrow 2Cr^{+3}$	$Cr_2O_7^{=} \rightarrow 2Cr(OH)_3$
$MnO_4^{-} \rightarrow Mn^{+2}$	$MnO_4^{-} \rightarrow MnO_2$

Also, the student should be reminded that in alkaline solution, the halogens, chlorine, bromine, and iodine, go over into halide plus hypohalite ions (e.g., $Cl_2 \rightarrow Cl^- + OCl^-$), CO_2 exists as $CO_3^{=}$, and acids will be in their salt or ionized forms.

Problem: Write a balanced equation for the oxidation of $CH_3—CHNH_2—CHBr—CHOH—CHOH—CH_3$ to $CH_3COOH + CO_2 + HOOC—CH_3 + N_2 + Br_2$ with potassium permanganate in alkaline solution.

Solution:

Step 1: First, the substances are written down in the form in which they will exist in the reaction mixture.

$$CH_3—CHNH_2—CHBr—CHOH—CHOH—CH_3 \rightarrow 2CH_3CO_2^- + CO_3^{=} + N_2 + Br^- + OBr^-$$

Carbon is balanced by using $2CO_3^{=}$, and nitrogen and bromine by using $\frac{1}{2}N_2$, $\frac{1}{2}Br^-$, and $\frac{1}{2}OBr^-$.

$$CH_3—CHNH_2—CHBr—(CHOH)_2—CH_3 \rightarrow 2CH_3CO_2^- + 2CO_3^{=} + \tfrac{1}{2}N_2 + \tfrac{1}{2}Br^- + \tfrac{1}{2}OBr^-$$

Although the author uses fractions, he finds that most students prefer to avoid them, so that fractions will be eliminated here. To do this, multiply everything by 2.

$$2CH_3—CHNH_2—CHBr—(CHOH)_2—CH_3 \rightarrow 4CH_3CO_2^- + 4CO_3^{=} + N_2 + Br^- + OBr^- \quad (1)$$

Step 2: In equation (1) there are 4 oxygens on the left and 8 + 12 + 1 = 21 on the right side; so add 17 H_2O's to the left.

$$2CH_3CHNH_2—CHBr—(CHOH)_2—CH_3 + 17H_2O \rightarrow 4CH_3CO_2^- + 4CO_3^{=} + N_2 + Br^- + OBr^-$$

Now, there are 2 × 14 + 2 × 17 = 62 hydrogens on the left side and 4 × 3 = 12 on the right; so add 62 − 12 = 50 H^+'s to the right.

$$17H_2O + 2CH_3—CHNH_2—CHBr—(CHOH)_2—CH_3 \rightarrow 4CH_3CO_2^- + 4CO_3^{=} + N_2 + Br^- + OBr^- + 50H^+ \quad (2)$$

Step 3: There are no ionic charges on the left side and $-4 + (-8) + (-2) + 50 = 36$ positive charges on the right; so 36 electrons are added to the right side.

$$17H_2O + 2CH_3{-}CHNH_2{-}CHBr{-}(CHOH)_2CH_3 \rightarrow$$
$$4CH_3CO_2^- + 4CO_3^= + N_2 + Br^- + OBr^- + 50H^+ + 36e^- \quad (3)$$

(It will be found that electrons always go on the same side as the protons.)

Step 4: Equation (3) is balanced, but it is improper to have excess protons in an alkaline medium; so Step 4 is employed. In this case, 50 hydroxide ions are added to both sides of the arrow, but $50H^+$ and $50(OH^-)$ are immediately equivalent to 50 H_2O's; so now 17 H_2O's may be subtracted from each side.

$$50(OH^-) + \cancel{17H_2O} +$$
$$2CH_3{-}CHNH_2{-}CHBr{-}(CHOH)_2{-}CH_3 \rightarrow$$
$$4CH_3CO_2^- + 4CO_3^= + N_2 + Br^- + OBr^- +$$
$$36e^- + \underbrace{\cancel{50H^+ + 50(OH^-)}}_{33\,\cancel{50}H_2O} \quad (4)$$

Now for the permanganate half-reaction.

Step 1: $MnO_4^- \rightarrow MnO_2$

Step 2: 4 Oxygens on the left and 2 on the right; so add 2 H_2O's to the right side.

$$MnO_4^- \rightarrow MnO_2 + 2H_2O$$

Now, 4 H^+'s are added to the left.

$$4H^+ + MnO_4^- \rightarrow MnO_2 + 2H_2O$$

Step 3: $+4 - 1 = +3$ charges on the left; so add 3 electrons to the left.

$$3e^- + 4H^+ + MnO_4^- \rightarrow MnO_2 + 2H_2O$$

Step 4: Add 4 (OH^-)'s to both sides and cancel 2 H_2O's.

$$3e^- + \underbrace{\cancel{4(OH^-)} + \cancel{4H^+}}_{2\,\cancel{4}H_2O} + MnO_4^- \rightarrow MnO_2 + \cancel{2H_2O} + 4(OH^-) \quad (5)$$

Now, combine half-reactions (4) and (5). The lowest common denominator (LCD) is 36; hence 36/36 = 1 times equation 4 and 36/3 = 12 times equation 5. 12 × equation 5 gives us:

$$36e^- + 24H_2O + 12MnO_4^- \rightarrow 12MnO_2 + 48(OH^-). \quad (6)$$

Upon adding equations 4 and 6, and canceling items occurring on both sides of the arrow, one gets

$$12MnO_4^- + 2(OH^-) + 2CH_3{-}CHNH_2{-}CHBr{-}(CHOH)_2{-}CH_3 \rightarrow$$
$$12MnO_2 + 4CH_3CO_2^- + 4CO_3^= + N_2 + Br^- + OBr^- + 9H_2O \quad (7)$$

Equation 7 should be balanced. For a check, examine the charges. There are $-12 + (-2) = -14$ on the left, and $-4 + (-8) + (-1) + (-1) = -14$ on the right.

Of course, in actual practice, the equations need not be repeated as often as was done here; it was done merely to clarify the explanations.

Problem: What weight of potassium dichromate would be required to oxidise one mole of $\mathrm{CH_3{-}CH{=}CH{-}CH_2{-}CHNH_2{-}CH_3}$ to $\mathrm{CH_3{-}CHOH{-}CHOH{-}CH_2{-}CO{-}CH_3 + N_2}$ in acid solution?

Solution: In this problem, one need not write a completely balanced equation but merely find the electron change for the two reactants so that their molar reacting ratio may be ascertained.

Step 1: In this case, carbon is already balanced when the substances are written down, and nitrogen is balanced by using 2 moles of the organics.

$$\mathrm{2CH_3CH{=}CHCH_2CHNH_2CH_3 \rightarrow 2CH_3CHOH{-}CHOH{-}CH_2{-}CO{-}CH_3 + N_2}$$

Step 2: No O's on the left and 2 × 3 = 6 on the right; so add 6 $\mathrm{H_2O}$'s to the left.

$$\mathrm{6H_2O + 2CH_3CH{=}CHCH_2CHNH_2CH_3 \rightarrow 2CH_3{-}(CHOH)_2{-}CH_2{-}CO{-}CH_3 + N_2}$$

Now there are $2 \times 6 + 2 \times 13 = 38$ H's on the left, and $2 \times 12 = 24$ on the right; so add $38 - 24 = 14$ $\mathrm{H^+}$'s to the right.

$$\mathrm{6H_2O + 2CH_3CH{=}CHCH_2{-}CHNH_2{-}CH_3 \rightarrow 2CH_3{-}(CHOH)_2{-}CH_2COCH_3 + N_2 + 14H^+}$$

Step 3: No ionic charges are on the left and 14 on the right; hence add 14 electrons to the right

$$\mathrm{6H_2O + 2CH_3CH{=}CHCH_2CHNH_2CH_3 \rightarrow 2CH_3(CHOH)_2CH_2COCH_3 + N_2 + 14H^+ + 14}e^- \quad (1)$$

Now, for the dichromate salt,

Step 1: $\mathrm{Cr_2O_7^{=} \rightarrow 2Cr^{+3}}$

Step 2: $\mathrm{Cr_2O_7^{=} \rightarrow 2Cr^{+3} + 7H_2O}$

$$\mathrm{14H^+ + Cr_2O_7^{=} \rightarrow 2Cr^{+3} + 7H_2O}$$

Step 3: $+14 - 2 = 12$ positive charges on the left and $2 \times (+3) = +6$ on the right; so add 6 electrons to the left.

$$6e^- + \mathrm{14H^+ + Cr_2O_7^{=} \rightarrow 2Cr^{+3} + 7H_2O} \quad (2)$$

The LCD for electrons in equations (1) and (2) is 42. However, we need not multiply equations (1) and (2) throughout by the quotients; we only want to find out what numbers of moles of the oxidant and reductant are involved. Hence, $42/14 = 3$, or $3 \times 2 = 6$ moles of $\mathrm{CH_3CH{=}CH{-}CH_2{-}CHNH_2{-}CH_3}$, and $42/6 = 7$ moles of $\mathrm{Cr_2O_7^{=}}$. This indicates that 7 moles of $\mathrm{K_2Cr_2O_7}$ are required to oxidize 6 moles of $\mathrm{CH_3{-}CH{=}CH{-}CH_2{-}CHNH_2{-}CH_3}$ to the indicated products. Thus, to answer the initial problem, if it takes 7 moles of dichromate for 6 moles of the organic compound, it would take 7/6 moles of $\mathrm{K_2Cr_2O_7}$ for 1 mole of the organic compound $= 7/6 \times (294) = 343$ g.

Problem: Write a balanced equation for the reduction of nitrobenzene, $\mathrm{C_6H_5NO_2}$, to azobenzene, $\mathrm{C_6H_5N{=}NC_6H_5}$, with $\mathrm{LiAlH_4}$. Assume that $\mathrm{LiAlH_4}$ goes to $\mathrm{LiOH + Al(OH)_3}$.

Solution:

Step 1: $\mathrm{2C_6H_5NO_2 \rightarrow C_6H_5N{=}NC_6H_5}$

Step 2: $2C_6H_5NO_2 \rightarrow (C_6H_5N)_2 + 4H_2O$

10 H's on left $\quad$ $10 + 8 = 18$ H's on right

$8H^+ + 2C_6H_5NO_2 \rightarrow (C_6H_5N)_2 + 4H_2O$

Step 3: $8H^+ + 8e^- + 2C_6H_5NO_2 \rightarrow (C_6H_5N)_2 + 4H_2O$

Step 4: $\underbrace{\cancel{8(OH^-) + 8H^+}}_{4\,\cancel{8}H_2O} + 8e^- + 2C_6H_5NO_2 \rightarrow (C_6H_5N)_2 + \cancel{4H_2O} + 8(OH^-)$

$$4H_2O + 8e^- + 2C_6H_5NO_2 \rightarrow (C_6H_5N)_2 + 8(OH^-) \qquad (1)$$

For $LiAlH_4$:

Step 1: $LiAlH_4 \rightarrow LiOH + Al(OH)_3$

Step 2: $4H_2O + LiAlH_4 \rightarrow LiOH + Al(OH)_3$

$4H_2O + LiAlH_4 \rightarrow LiOH + Al(OH)_3 + 8H^+$

Step 3: $4H_2O + LiAlH_4 \rightarrow LiOH + Al(OH)_3 + 8H^+ + 8e^-$

Step 4: $8(OH^-) + \cancel{4H_2O} + LiAlH_4 \rightarrow LiOH + Al(OH)_3 + 8e^- + \underbrace{\cancel{8H^+ + 8(OH^-)}}_{4\,\cancel{8}H_2O}$

$$8(OH^-) + LiAlH_4 \rightarrow LiOH + Al(OH)_3 + 8e^- + 4H_2O \qquad (2)$$

Both half-reactions involve 8 electrons so the half-reactions may be added directly. If 4 H_2O's, 8 electrons, and 8 (OH^-)'s are subtracted from both sides of the arrow, one gets

$$2C_6H_5NO_2 + LiAlH_4 \rightarrow C_6H_5N{=}NC_6H_5 + LiOH + Al(OH)_3.$$

Problem: Write a balanced equation for the oxidation of $C_6H_5CH{=}CH{-}CH_3$ to $C_6H_5CHO + CH_3CHO$ with nitrobenzene, $C_6H_5NO_2$, in alkaline solution (the nitrobenzene is reduced to aniline, $C_6H_5NH_2$).

Solution:

Step 1: $C_6H_5CH{=}CH{-}CH_3 \rightarrow C_6H_5CHO + CH_3CHO$

Step 2: $2H_2O + C_6H_5CH{=}CHCH_3 \rightarrow C_6H_5CHO + CH_3CHO$

$4 + 10 = 14$ H's $\quad$ 10 H's

$2H_2O + C_6H_5CH{=}CHCH_3 \rightarrow C_6H_5CHO + CH_3CHO + 4H^+$

Step 3: $2H_2O + C_6H_5CH{=}CHCH_3 \rightarrow C_6H_5CHO + CH_3CHO + 4H^+ + 4e^-$

Step 4: $4(OH^-) + \cancel{2H_2O} + C_6H_5CH{=}CHCH_3 \rightarrow$

$C_6H_5CHO + CH_3CHO + 4e^- + \underbrace{\cancel{4H^+ + 4(OH^-)}}_{2\,\cancel{4}H_2O}$

For $C_6H_5NO_2$:

Step 1: $C_6H_5NO_2 \rightarrow C_6H_5NH_2$

Step 2: $C_6H_5NO_2 \rightarrow C_6H_5NH_2 + 2H_2O$

5 H's $\quad$ $7 + 4 = 11$ H's

$6H^+ + C_6H_5NO_2 \rightarrow C_6H_5NH_2 + 2H_2O$

Step 3: $6e^- + 6H^+ + C_6H_5NO_2 \rightarrow C_6H_5NH_2 + 2H_2O$

Step 4: $6e^- + \underbrace{\cancel{6H^+} + \cancel{6(OH^-)}}_{4\,\cancel{6}H_2O} + C_6H_5NO_2 \rightarrow C_6H_5NH_2 + 2H_2O + 6(OH^-)$

LCD = 12, hence,

$$\cancel{12(OH^-)} + 3C_6H_5CH{=}CHCH_3 \rightarrow 3C_6H_5CHO + 3CH_3CHO + \cancel{12e^-} + 6H_2O$$

$$\cancel{12e^-} + 2\,\cancel{8}H_2O + 2C_6H_5NO_2 \rightarrow 2C_6H_5NH_2 + \cancel{12(OH^-)}$$

$$3C_6H_5CH{=}CHCH_3 + 2H_2O + 2C_6H_5NO_2 \rightarrow 3C_6H_5CHO + 3CH_3CHO + 2C_6H_5NH_2$$

Valence-change method. If one can assign tentative oxidation numbers to carbon atoms in organic compounds, then the valence change method may be used and often takes less time than the method illustrated above. The assignment of oxidation numbers to elements is merely for convenience and is entirely arbitrary.[10] One scheme that is fairly simple is the following.[11] One assumes oxidation numbers of −2 for oxygen, +1 for hydrogen, and zero for all other elements in organic compounds except carbon. Use molecular formulas for convenience.

Illustration: Write a balanced equation for the oxidation of $CH_3{-}CHOH{-}CH_2{-}CH{=}CH{-}CH_2OH$ to $CH_3{-}CO{-}CH_2{-}COOH + CO_2$ with potassium dichromate in acid solution.

Solution: The small numbers appearing above molecular formulas refer to the gross oxidation numbers assigned to the respective elements.

$$\overset{-8+12-4}{C_6H_{12}O_2} \rightarrow \overset{0+6-6}{C_4H_6O_3} + \overset{+4-4}{2CO_2} \qquad \text{(a)}$$

That is, if each oxygen is −2 and hydrogen +1, then to be neutral, the 6 C's in $C_6H_{12}O_2$ must collectively contribute −8 charges; the 4 C's in $C_4H_6O_3$ must have zero charge, and the C in CO_2 must have an oxidation number of +4. Collectively, the carbon atoms undergo an electron change from −8 to $0 + 2(+4) = 16$ electrons. For dichromate, we have as usual:

$$6e^- + Cr_2O_7^{=} \rightarrow 2Cr^{+3} \qquad \text{(b)}$$

Hence, the LCD between 6 and 16 electrons is 48; so,

$$48/16 \times \text{(a) gives } 3C_6H_{12}O_2 \rightarrow 3C_4H_6O_3 + 6CO_2$$

$$48/6 \times \text{(b) gives } 8Cr_2O_7^{=} \rightarrow 16Cr^{+3}$$

$$3C_6H_{12}O_2 + 8Cr_2O_7^{=} \rightarrow 3C_4H_6O_3 + 6CO_2 + 16Cr^{+3} \qquad (1)$$

To balance this, bring oxygen to a balance with H_2O, then hydrogen to a balance with protons. There are $3 \times 2 + 8 \times 7 = 62$ O's on the left, and $3 \times 3 + 6 \times 2 = 21$ O's on the right side; hence, $62 - 21 = 41$ H_2O's are added to the right.

$$3C_6H_{12}O_2 + 8Cr_2O_7^{=} \rightarrow 3C_4H_6O_3 + 6CO_2 + 6Cr^{+3} + 41H_2O$$

[10] Cf. D. F. Swinehart, *J. Chem. Education* **29**, 284 (1952); G. W. Bennett, *ibid.* **31**, 157 (1954).

[11] The author is indebted to Professor Moddie D. Taylor for this scheme.

Now, since there are 3 × 12 = 36 H's on the left and 3 × 6 + 41 × 2 = 100 H's on the right side, add 100 − 36 = 64 H^+ ions to the left side.

$$64H^+ + 3C_6H_{12}O_2 + 8Cr_2O_7^{=} \rightarrow 3C_4H_6O_3 + 6CO_2 + 16Cr^{+3} + 41H_2O \qquad (2)$$

This is the final balanced equation and an examination of charges reveals that they check: +64 + (−16) = +48 on the left, and 16 × (+3) = +48 on the right.

Problem: What weight of potassium permanganate is required to oxidize 50 g. of cinnamaldehyde, $C_6H_5CH{=}CH{-}CHO$, to benzoic acid, C_6H_5COOH, and CO_2 in alkaline solution, if the permanganate is only 95% pure?

Solution: Again, one merely wishes to know the reacting molar ratio between the cinnamaldehyde and the potassium permanganate for this reaction. Sufficient $KMnO_4$ is used to provide the required number of equivalents of oxidant.

Step 1: $$\overset{-6+8-2}{C_9H_8O} \rightarrow \overset{-2+5-4}{C_7H_5O_2} + \overset{+4-6}{2CO_3} + 12e^-$$

Step 2: $$3e^- + MnO_4^- \rightarrow MnO_2$$

Step 3: $$C_9H_8O + 4MnO_4^- \rightarrow 4MnO_2 + C_7H_5O_2^- + 2CO_3^{=}$$

Therefore 4 moles of potassium permanganate are required per mole of cinnamaldehyde. The molecular weight of the latter is 132; hence, 4 × (50/132) moles of $KMnO_4$ (mol. wt. = 158) are required. Inasmuch as the potassium permanganate is only 95% pure, the weight to be used is

$$4 \times \frac{50}{132} \times 158 \times \frac{100}{95} = 252 \text{ g.}$$

In cases where it is clear that one portion of a molecule does not undergo a change, this portion may be neglected when assigning oxidation numbers. For example, if $C_6H_5CH_3$ is oxidized to C_6H_5COOH, then the C_6H_5 need not be considered.

$$C_6H_5\overset{-3+3}{CH_3} \rightarrow C_6H_5{-}\overset{+3-4+1}{CO_2H}$$

$$-3 \rightarrow +3 = 6 \text{ electrons gained}$$

On the other hand, if a gross oxidation number for carbon in these compounds had been assigned, the same electron change results.

$$\overset{-8+8}{C_7H_8} \rightarrow \overset{-2+6-4}{C_7H_6O_2}$$

$$-8 \rightarrow -2 = 6 \text{ electrons gained}$$

Problem: What weight of $KMnO_4$ would be required to oxidize 100 g. of crude acetophenone to benzoic acid in acid solution if the $KMnO_4$ is only 96% pure? To ascertain the acetophenone-content of the crude material, a 5-g. sample from the same stock was reacted with excess 2,4-dinitrophenylhydrazine reagent and 9.99 g. of the 2,4-dinitrophenylhydrazone was precipitated.

Solution: One needs to know the reaction ratio between $KMnO_4$ and acetophenone, and how much acetophenone is actually in the 100 g. of crude material. The latter fact is obtainable from the amount of 2,4-dinitrophenylhydrazone produced from the 5-g. sample.

$$\underset{120}{\overset{X}{C_6H_5COCH_3}} + H_2N{-}NHC_6H_3(NO_2)_2 \rightarrow \underset{300}{\overset{9.99\text{ g.}}{C_6H_5C(CH_3){=}N{-}NHC_6H_3(NO_2)_2}}$$

From the equation for the reaction and the molecular weights, one has the ratio, where X is the weight of acetophenone in the 5-g. sample,

$$\frac{X}{120} = \frac{9.99}{300}, \qquad X = 4\text{ g.}$$

Hence, 5 g. of crude material contains 4 g. of acetophenone. Accordingly, 100 g. of crude material contain:

$$\frac{4}{5} = \frac{Y}{100}, \qquad Y = 80\text{ g.}$$

Now, to get the reacting molar ratio between $KMnO_4$ and acetophenone:

$$\overset{-1+3-2}{C_6H_5C_2H_3O} \rightarrow \overset{+3-4+1}{C_6H_5CO_2H} + \overset{+4-4}{CO_2}$$

$$-1 \xrightarrow{-8e^-} +7$$

$$MnO_4^- \xrightarrow{-5e^-} Mn^{+2}$$

LCD = 40, and the ratio is $5C_6H_5COCH_3$ to $8KMnO_4$

This gives the ratio:

$$\frac{80}{5(120)} = \frac{Z}{8(158)}, \qquad Z = 169\text{ g.}$$

However, since the $KMnO_4$ is only 96% pure, the actual amount to be weighed out and used is

$$169\,\frac{(100)}{96} = 176\text{ g.}$$

EXERCISES

1. Write balanced equations for the oxidation of toluene to benzoic acid with potassium permanganate in acid and alkaline solutions.

Ans. $6MnO_4^- + 5C_6H_5CH_3 + 18H^+ \rightarrow 5C_6H_5CO_2H + 6Mn^{+2} + 14H_2O$
$2MnO_4^- + C_6H_5CH_3 \rightarrow C_6H_5CO_2^- + 2MnO_2 + OH^- + H_2O$

2. Write a balanced equation for the reduction of nitrobenzene with iron in acid solution. Assume that the iron is oxidized to ferric ion and the nitrobenzene is reduced to aniline ($C_6H_5NH_3^+$ in acid solution).

Ans. $2Fe + C_6H_5NO_2 + 7H^+ \rightarrow C_6H_5NH_3^+ + 2Fe^{+3} + 2H_2O$

3. What weight of potassium permanganate would be required to oxidize 100 g. of naphthalene to phthaldehydic acid (*o*-formylbenzoic acid) with $KMnO_4$ in alkaline solution?

Ans. $3C_{10}H_8 + 16MnO_4^- \rightarrow 4H_2O + 16MnO_2 + OH^- + 6CO_3^= + 3OCH{-}C_6H_4{-}CO_2^-$
therefore, 658 g. of $KMnO_4$

4. What weight of CrO_3 would be used to oxidise 50 g. of *p*-nitrotoluene to *p*-nitrobenzal diacetate in acetic acid–acetic anhydride solution?

Ans. $12H^+ + 6AcOH + 3O_2NC_6H_4CH_3 + 4CrO_3 \rightarrow$
$4Cr^{+3} + 3O_2NC_6H_4CH(OAc)_2 + 12H_2O$

therefore, 48.6 g. of CrO_3

5. Write a balanced equation for the oxidation of CH_3—$CHOH$—CH_2—CHO to CH_3—CO—CH_2COOH with potassium dichromate in acid solution.

Ans. $16H^+ + 2Cr_2O_7^{=} + 3CH_3CHOHCH_2CHO \rightarrow$
$4Cr^{+3} + 11H_2O + 3CH_3COCH_2COOH$

6. Write a balanced equation for the oxidation of 2-hexene to 2,3-hexanediol with potassium permanganate in aq. sodium carbonate.

Ans. $4H_2O + 2MnO_4^- + 3CH_3CH_2CH_2CH{=}CHCH_3 \rightarrow$
$3CH_3CH_2CH_2(CHOH)_2—CH_3 + 2(OH^-) + 2MnO_2$

7. Write a balanced equation for the reduction of ethyl propionate to propyl alcohol and ethyl alcohol with sodium metal.

Ans. $4H_2O + 4Na + CH_3CH_2CO_2C_2H_5 \rightarrow$
$CH_3CH_2CH_2OH + C_2H_5OH + 4Na^+ + 4(OH^-)$

8. Write a balanced equation for the oxidation of ethyl alcohol to acetic acid with $KMnO_4$ in acid solution.

Ans. $12H^+ + 4MnO_4^- + 5CH_3CH_2OH \rightarrow 5CH_3COOH + 11H_2O + 4Mn^{++}$

9. What weight of potassium dichromate and *o*-xylene would be required to prepare 1 mole of phthalic acid if the per cent yield in the reaction is 85% and the potassium dichromate is 96% pure? *Ans.* 124 g. *o*-xylene; 720 g. $K_2Cr_2O_7$

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TABLE A.1 CONVERSIONS, CONSTANTS, AND FORMULAS

Volume and Weight

1 U. S. gallon = 8.34 lbs × Sp Gr
1 U. S. gallon = 0.84 Imperial gallon
1 cu ft of liquid = 7.48 gal
1 cu ft of liquid = 62.32 lbs × Sp Gr
Specific gravity of sea water = 1.025 to 1.03
1 cu meter = 264.5 gal
1 barrel (oil) = 42 gal

Capacity and Velocity

1 gpm = 449 cu ft per sec

$$\text{gpm} = \frac{\text{lbs per hour}}{500 \times \text{Sp. Gr.}}$$

gpm = 0.069 × boiler Hp
gpm = 0.7 × bbl/hour = 0.0292 bbl/day
gpm = 0.227 metric tons per hour
1 mgd = 694.5 gpm

$$V = \frac{\text{gpm} \times 0.321}{\text{area in sq. in}} = \frac{\text{gpm} \times 0.409}{D^2}$$

$$V = \sqrt{2gH}$$

gpm = gallons per minute
Sp Gr = specific gravity based on water at 62°F
Hp = horsepower
bbl = barrel (oil) = 42 gal
mgd = million gallons per day of 24 hours
V = velocity in ft/sec
D = diameter in inches
g = 32.16 ft/sec/sec
H = head in feet

Head

$$\text{Head in feet} = \frac{\text{Head in psi} \times 2.31}{\text{Sp Gr}}$$

1 foot water (cold, fresh) = 1.133 inches of mercury
1 psi = 0.0703 kilograms per sq centimeter
1 psi = 0.068 atmosphere

$$H = \frac{V^2}{2g}$$

psi = pounds per square inch

Power and Torque

1 horsepower = 550 ft-lb per sec
= 33,000 ft-lb per min
= 2545 btu per hr
= 745.7 watts
= 0.7457 kilowatts

$$\text{bhp} = \frac{\text{gpm} \times \text{Head in feet} \times \text{Sp Gr.}}{3960 \times \text{efficiency}}$$

$$\text{bhp} = \frac{\text{gpm} \times \text{Head in psi}}{1714 \times \text{efficiency}}$$

$$\text{Torque in lbs feet} = \frac{\text{Hp} \times 5252}{\text{rpm}}$$

bhp = brake horsepower
rpm = revolutions per minute

Miscellaneous Centrifugal Pump Formulas

$$\text{Specific speed} = N_S = \frac{\sqrt{\text{gpm}} \times \text{rpm}}{H^{3/4}}$$

where H = head per stage in feet

$$\text{Diameter of impeller in inches} = d = \frac{1840\ \text{Ku}\ \sqrt{H}}{\text{rpm}}$$

where Ku is a constant varying with impeller type and design. Use H at shut-off (zero capacity) and Ku is approx. 1.0

At constant speed:

$$\frac{d_1}{d_2} = \frac{\text{gpm}_1}{\text{gpm}_2} = \frac{\sqrt{H_1}}{\sqrt{H_2}} = \frac{\sqrt[3]{\text{bhp}_1}}{\sqrt[3]{\text{bhp}_2}}$$

At constant impeller diameter

$$\frac{\text{rpm}_1}{\text{rpm}_2} = \frac{\text{gpm}_1}{\text{gpm}_2} = \frac{\sqrt{H_1}}{\sqrt{H_2}} = \frac{\sqrt[3]{\text{Bhp}_1}}{\sqrt[3]{\text{Bhp}_2}}$$